核 磁 共 振 波 谱 学

Nuclear Magnetic Resonance (NMR) Spectroscopy

王　为

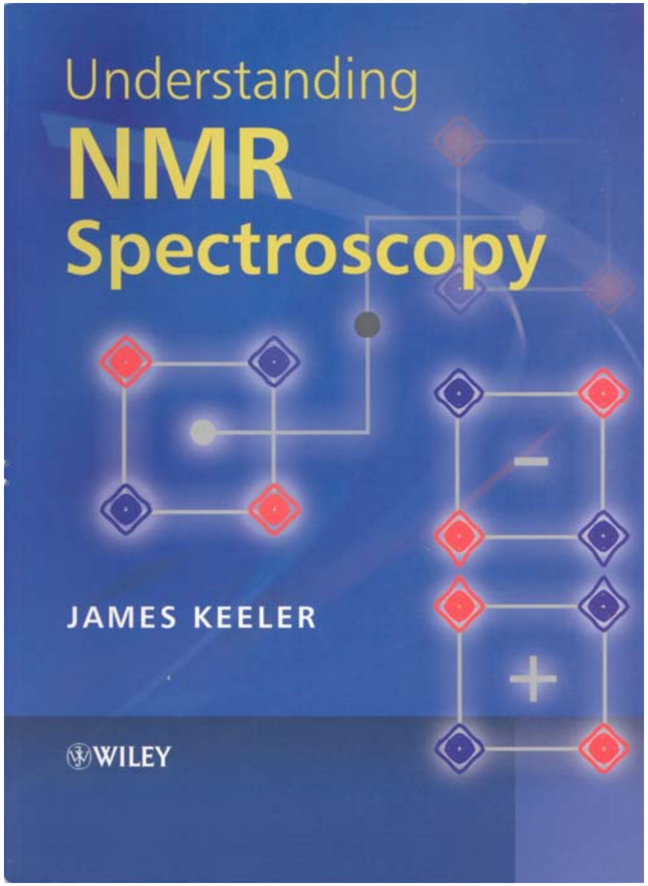
兰州大学化学化工学院

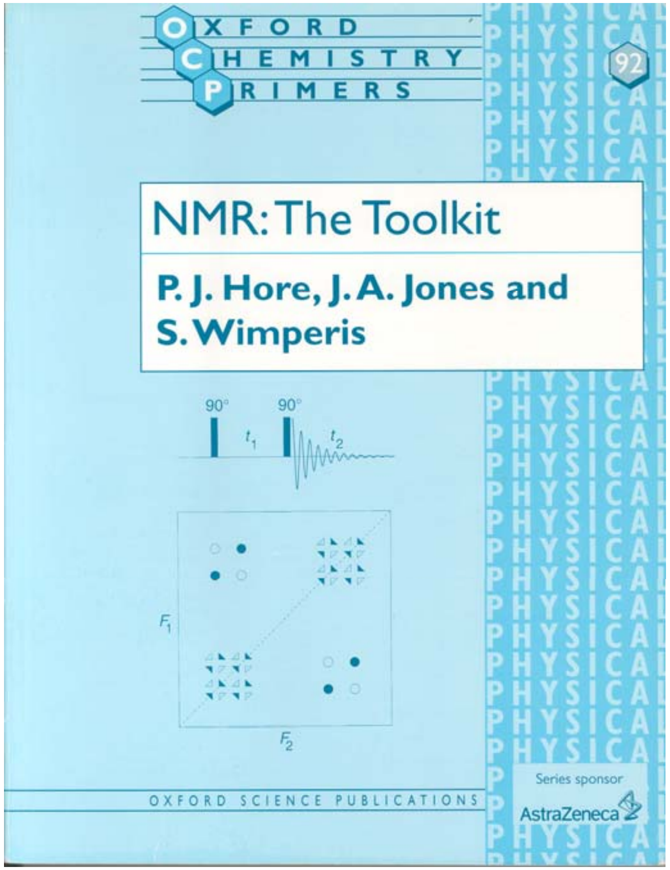
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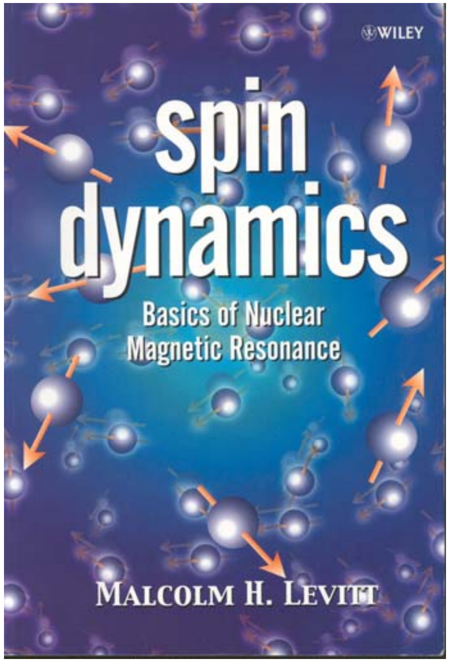
办公: 新化学楼**501**室

参考书目 (List of Reference Books)

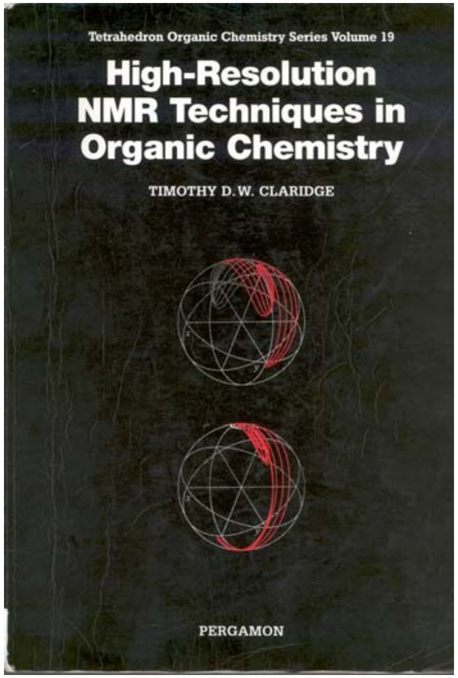




参考书目 (List of Reference Books)







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D. A. R. Williams, ***Nuclear Magnetic Resonance Spectroscopy***, Wiley, New York, 1986.

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E. Breitmaier, W. Voelter, ***^{13}C NMR Spectroscopy, 2nd Ed***. Verlag, New York, 1978.

R. M. Silverstein, F. X. Webster, ***Spectrometric Identification of Organic Compounds, 6th Ed***. Wiley, New York, 1998.

W. R. Croasmun, R. M. K. Carlson, ***Two-Dimensional NMR Spectroscopy***, VCH, New York,1987.

H. Duddeck, W. Dietrich, ***Structure Elucidation by Modern NMR***, Springer, New York,1989.

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近代核磁共振谱阐明结构, H. Duddeck *et al*. 著, 于德泉等译,
北京医科大学出版社, 1991年

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一维和二维核磁共振原理, R. R. Ernst *et al*. 著，毛希安译，
科学出版社 1997年

现代核磁共振实用技术及应用，毛希安，科技文献出版社, 2000年

有机化学中的光谱方法，王剑波等译，北京大学出版社, 2001年

Introduction

- **NMR history**
- **NMR spectrometer: structure, magnet, probe**
- **NMR safety**
- **Applications of NMR spectroscopy**

Important Events in Development of NMR

1938 Rabi, magnetic resonance for atomic nuclei (1944 Noble Prize);

1945 Bloch & Purcell, NMR phenomenon, (1952 Noble Prize);

1953 Varian Company, the first commercial NMR spectrometer;

1957 ^{13}C NMR;

1959 Solid state NMR;

1964 High resolution NMR (Superconducting magnet);

1965 Pulse Fourier Transform NMR (FT-NMR);

1967 Chemically Induced Dynamic Nuclear Polarization (CIDNP);

1976 Ernst, methodology in high resolution NMR (1991 Noble Prize);

1982 Lauterbur & Mansfield, Hospital NMR Imaging (2003 Nobel Prize);

1991 Wuethrich, NMR for bio-macromolecules (2002 Nobel Prize);

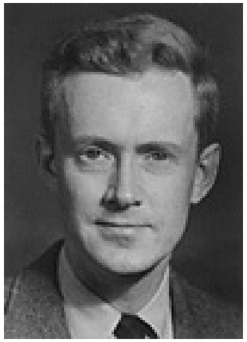
1995 LC-NMR, LC-MS-NMR

Nobel Prize Laureates Related to NMR

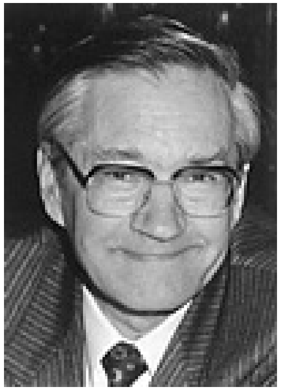


I. I. Rabi
1944, Physics
Resonance of nuclei





F. Bloch E. M. Purcell
1952, Physics
Discovery of NMR



R. R. Ernst
1991, Chemistry
HR & 2D NMR

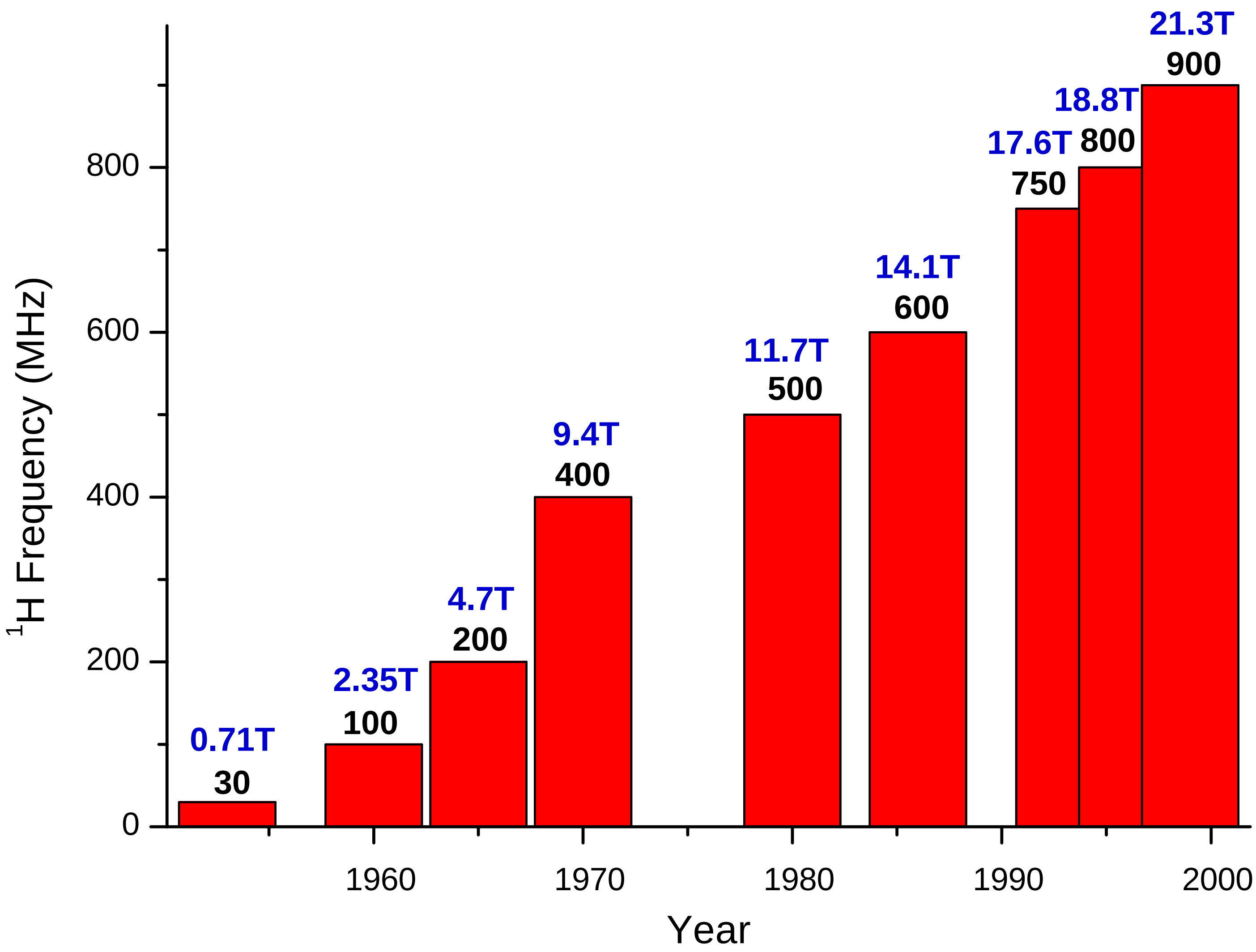


K. Wuethrich
2002, Chemistry
NMR for Bio-Macromol.

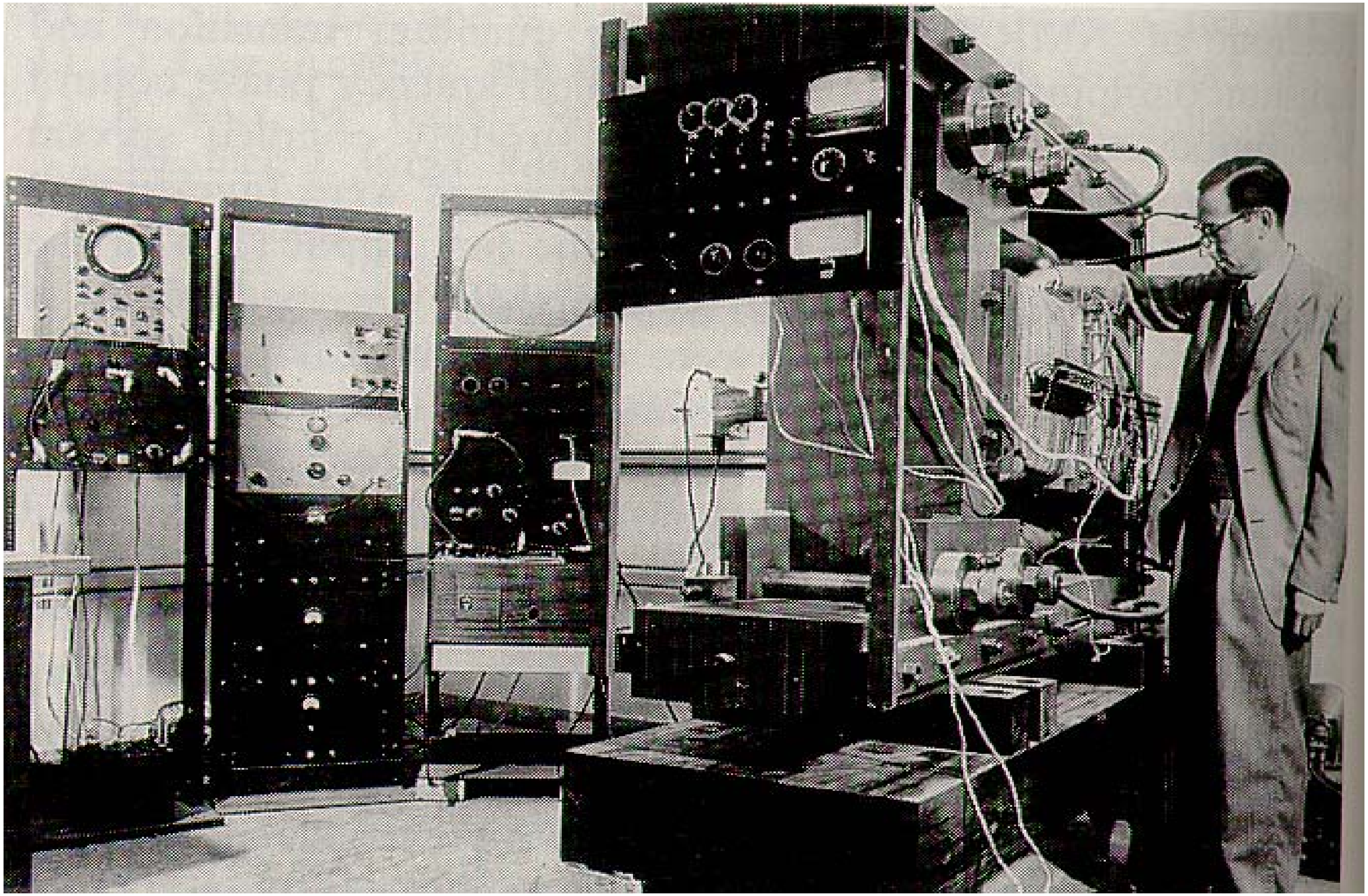


P. Lauterbur P. Mansfield
2003 Medicine
MRI

Increase of NMR Magnetic Field



1946: First NMR Signal in Stanford



Bloch’s Laboratory in Stanford, 1949

NMR Spectrometer in 1964



TRÜB-TÄUBER KIS-1

NMR Spectrometer in 1970



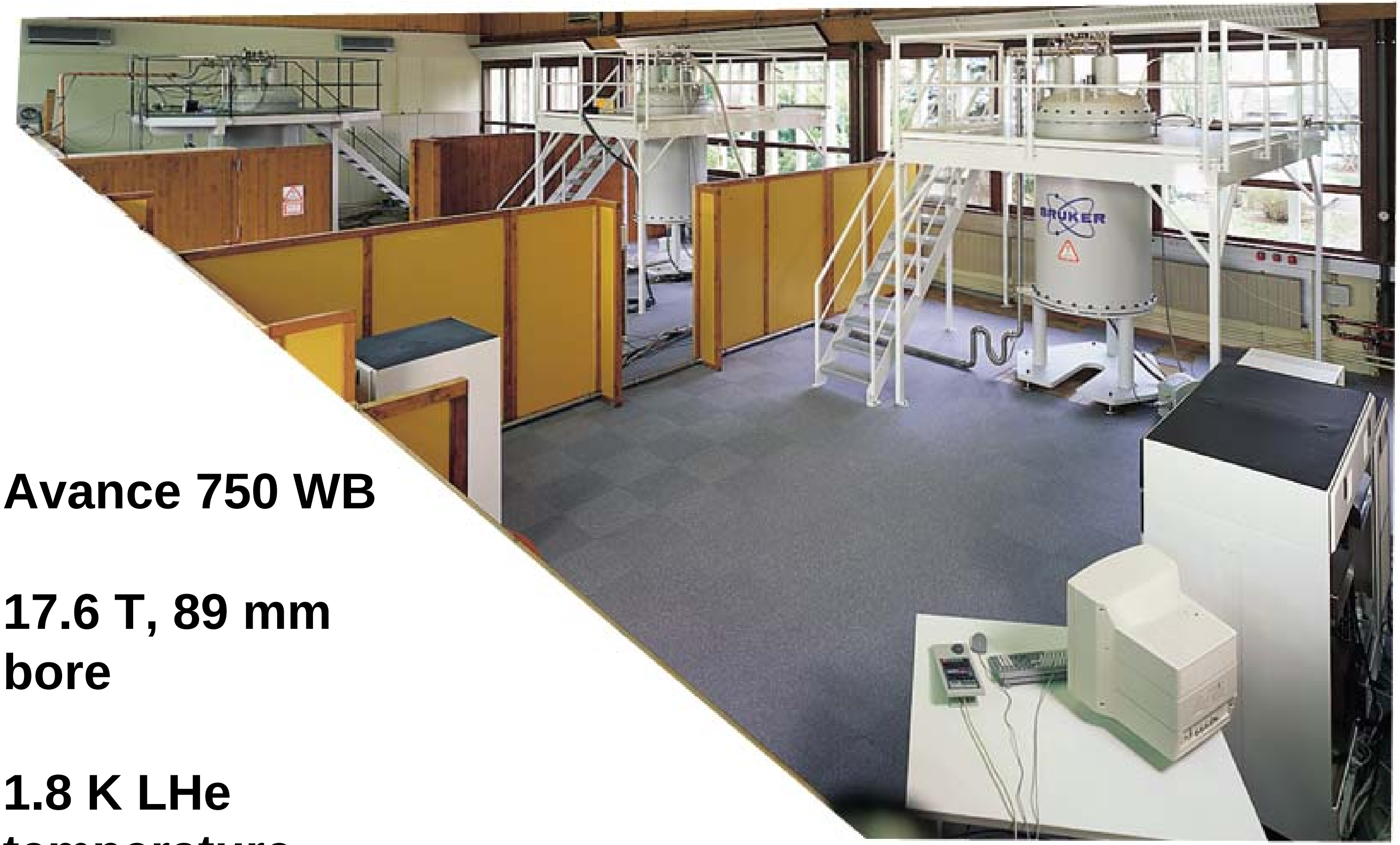
HFX90

NMR Spectrometer in 1985



AM console

Research NMR Spectrometer in 2000



Avance 750 WB

17.6 T, 89 mm bore

1.8 K LHe temperature

One of the NMR Spectrometers in SKLAOC, Lanzhou University



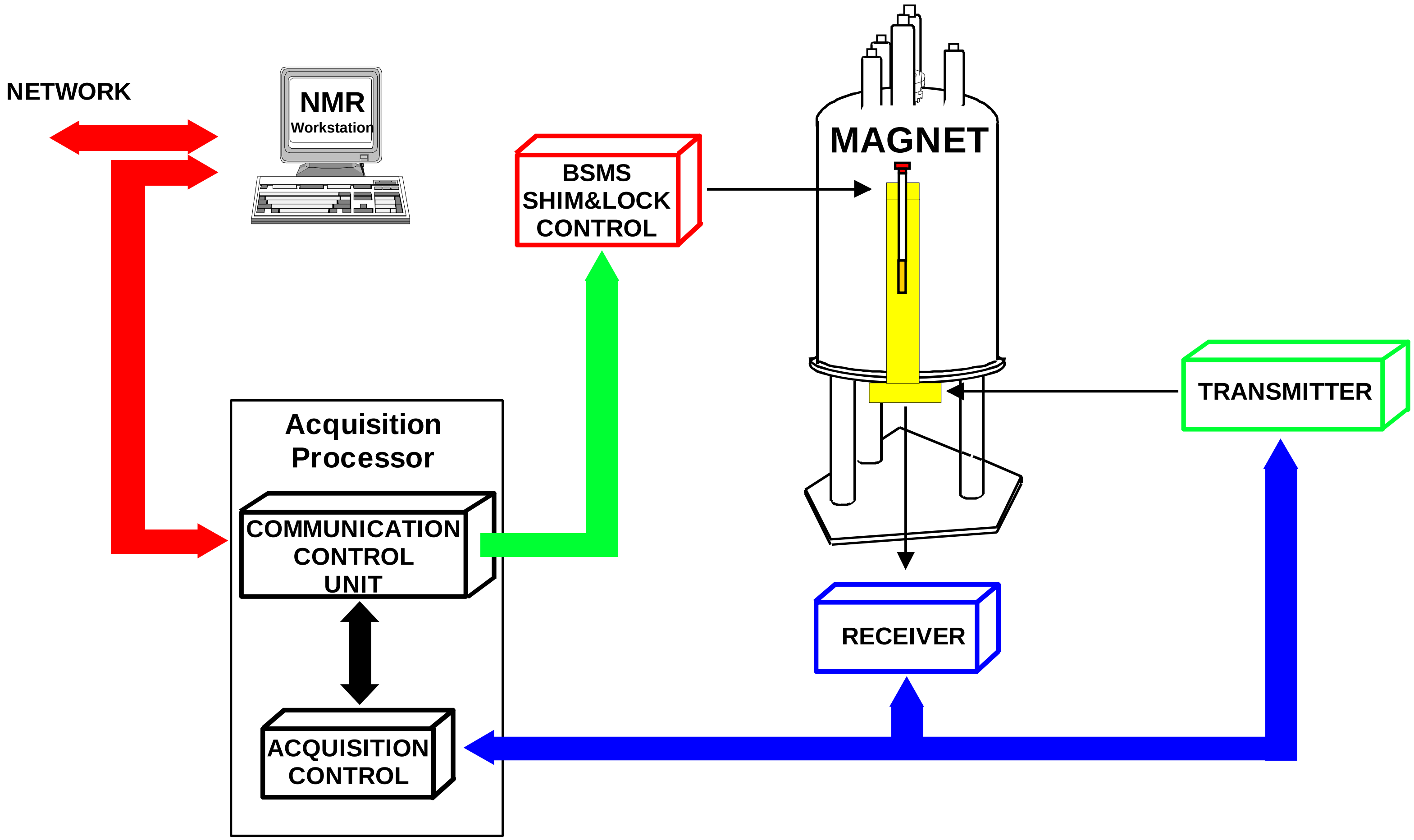
Varian INOVA 600

Solid-State NMR Spectrometer in SKLAOC, Lanzhou University

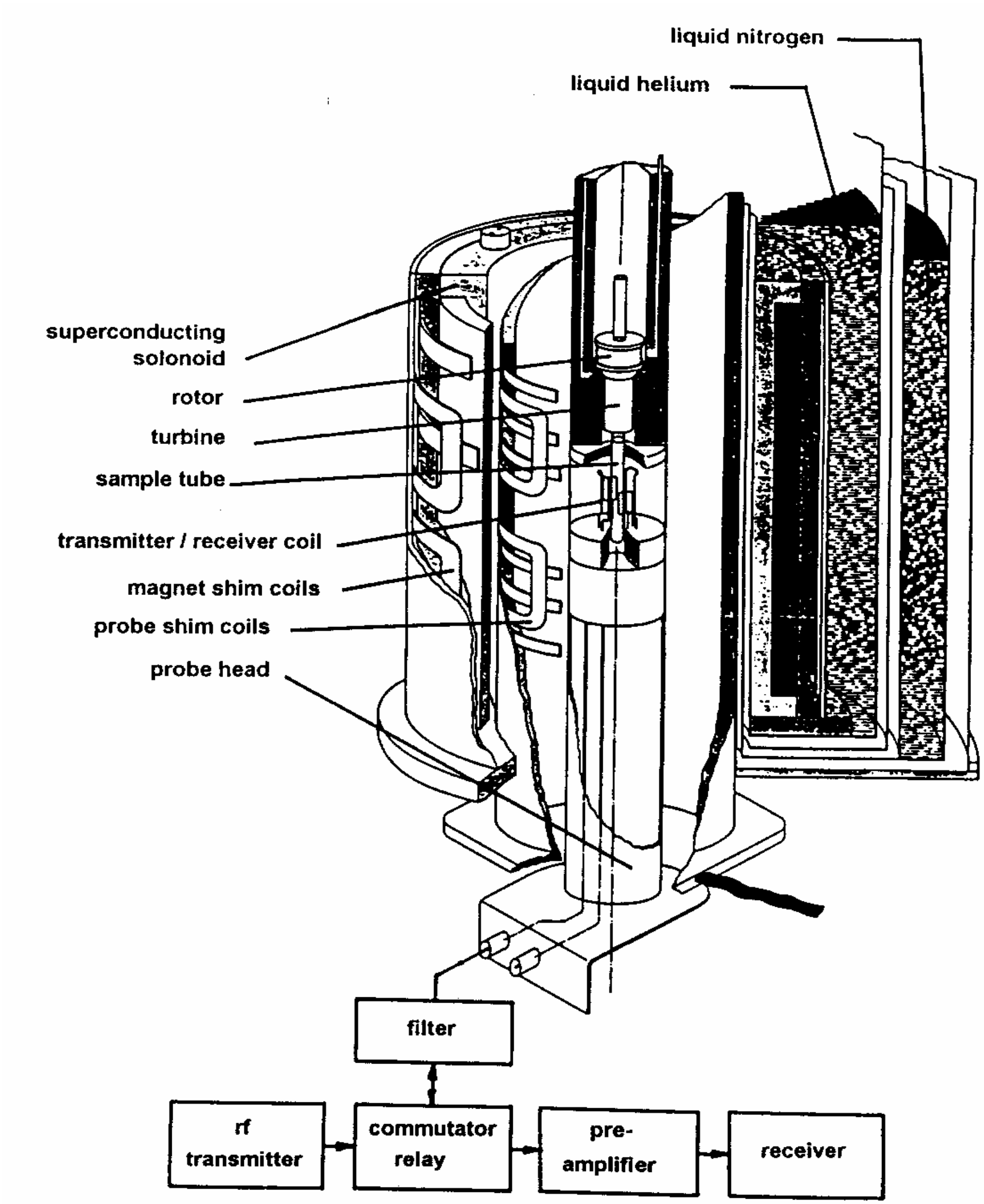


Bruker Avance 400 WB

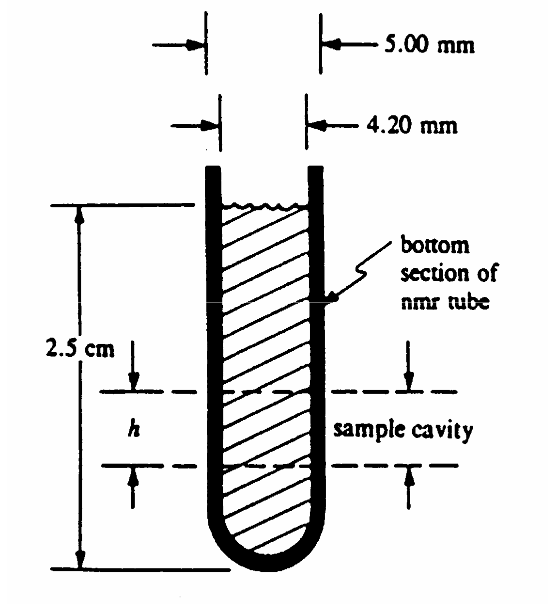
NMR Spectrometer Structure



NMR Magnet and Sample Tube



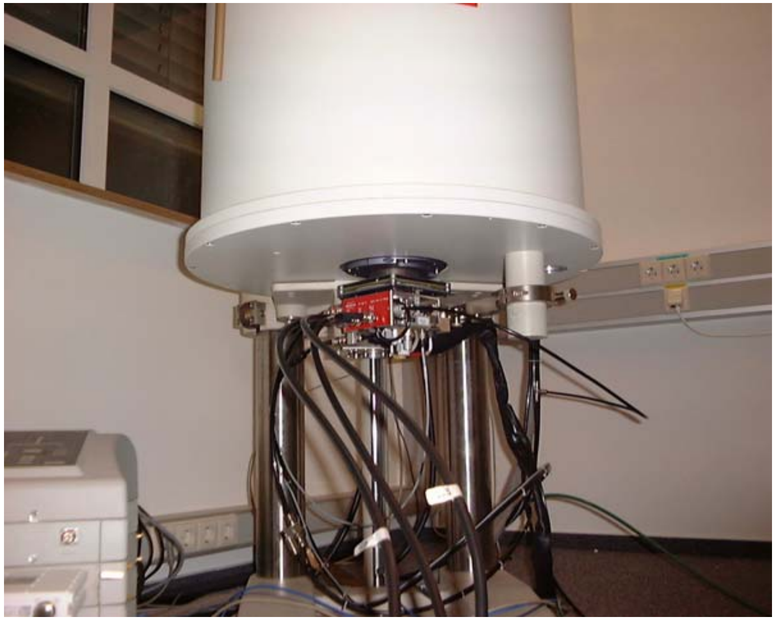
For Liquids



For Solids



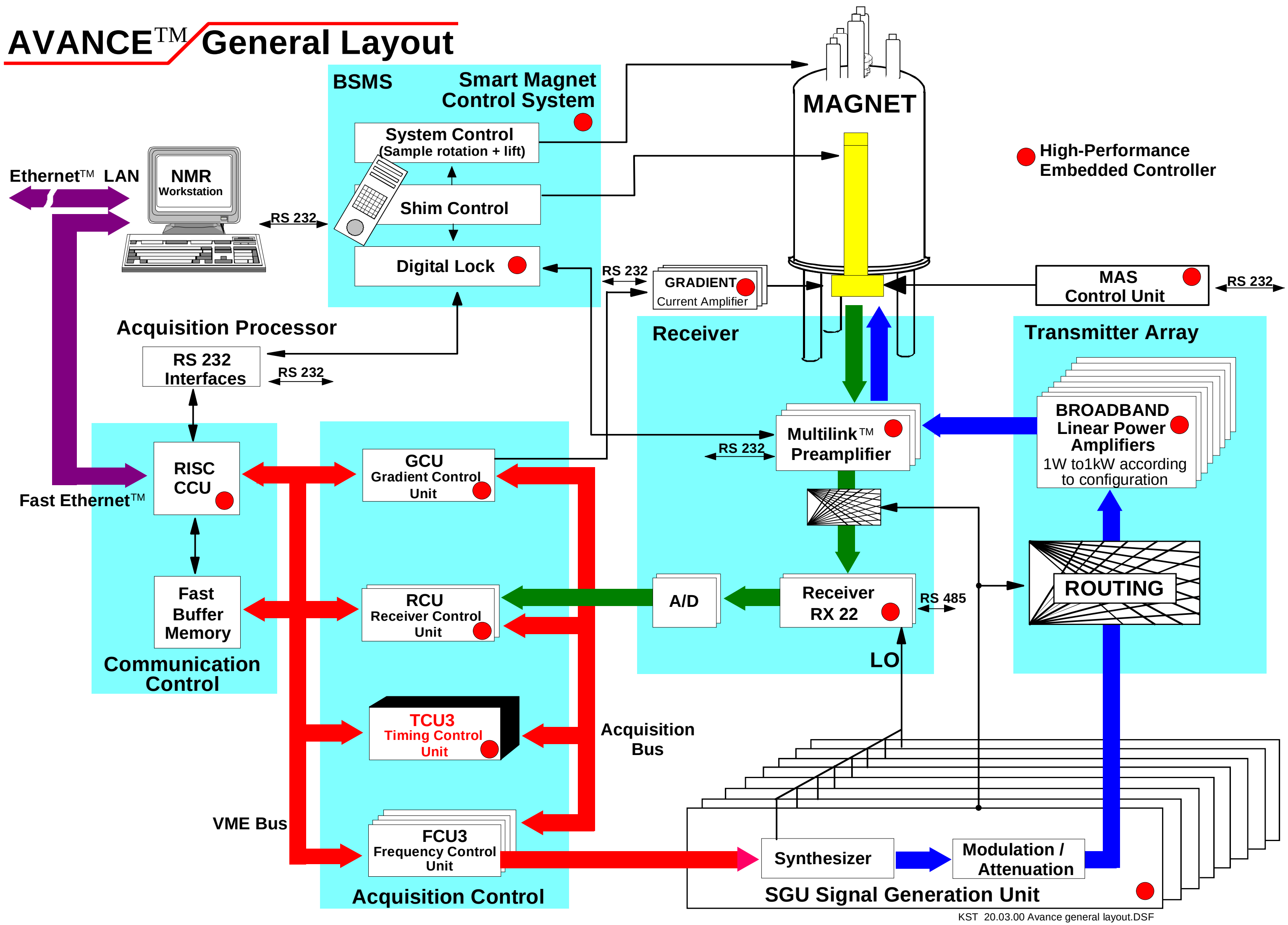
NMR Probe







NMR Spectrometer Structure



Safety Issues When Using NMR

5 Gauss line
Non-magnetic tools
Helium
Nitrogen

Warning Signs

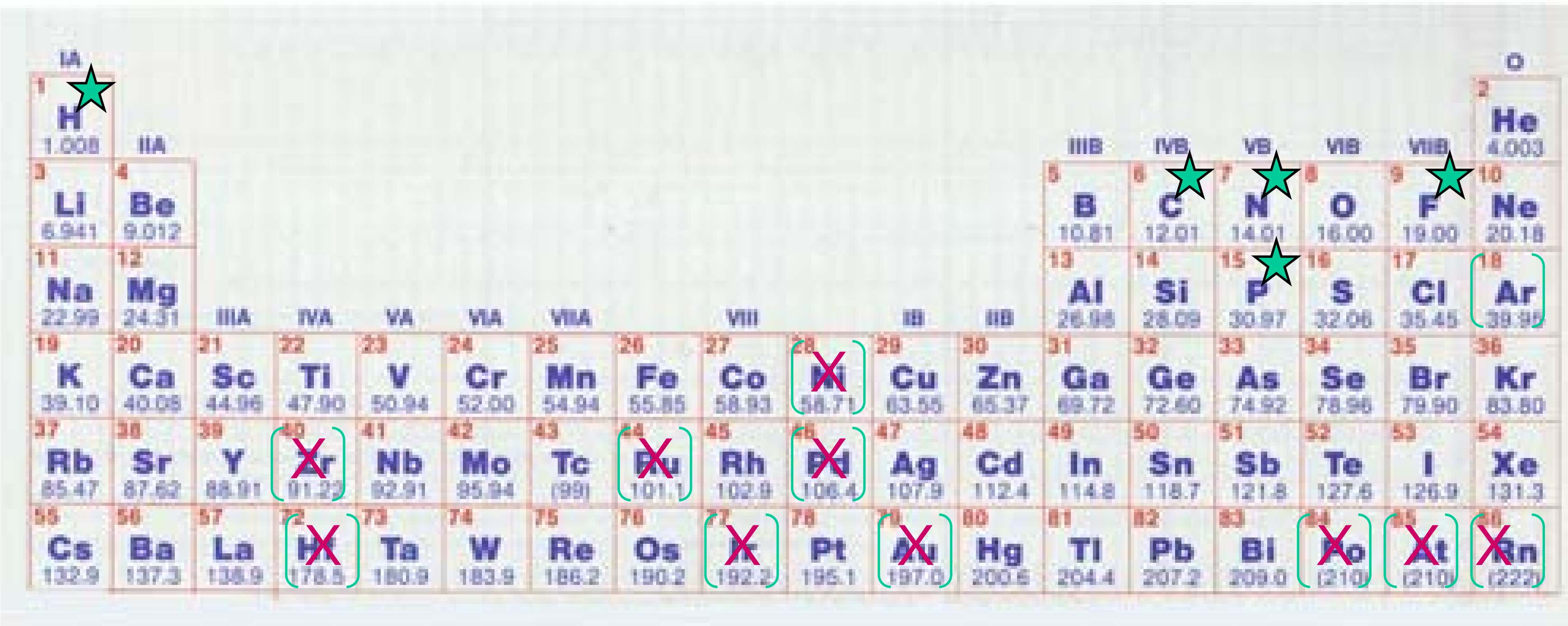




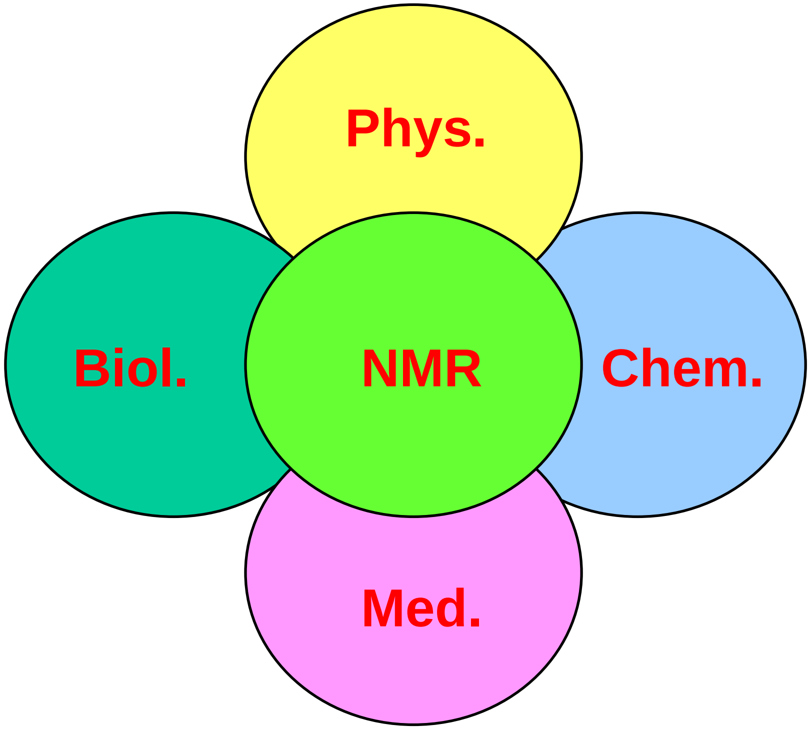
Magnet Quench



NMR Periodic Table of Elements



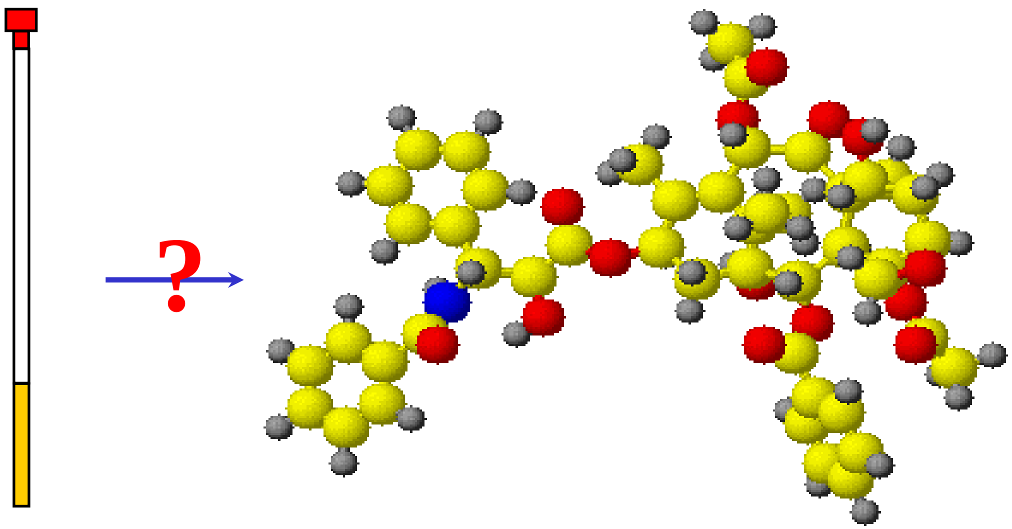
Applications of NMR

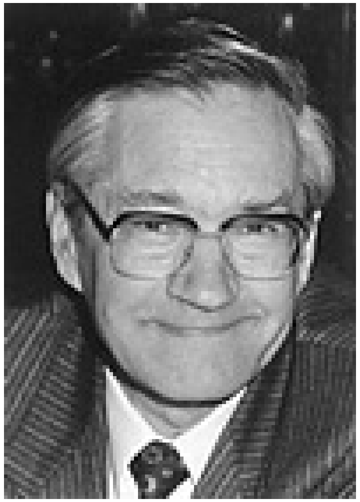


Applications of NMR

Molecular Structure in Solution

High resolution 1D & 2D NMR

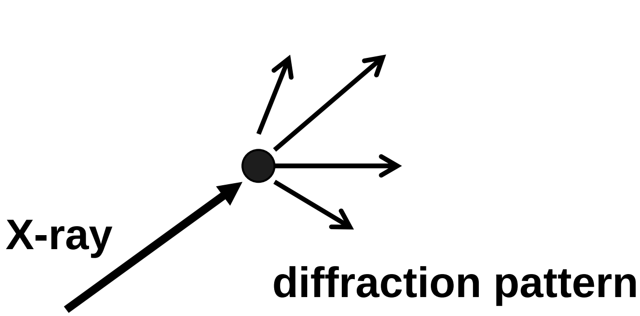


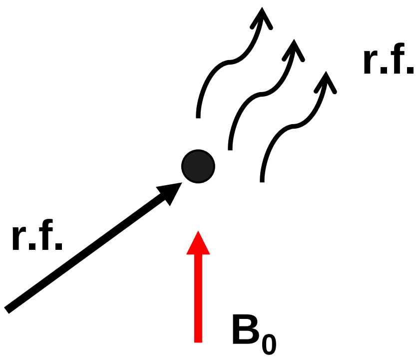


R. R. Ernst

1991 Nobel Prize
in Chemistry

Comparison of X-Ray and NMR





<u>X-ray</u>

Direct detection of atomic positions though electron density maps.

The globe structure is provided though each individual diffraction spot.

It requires high quality single crystals.

<u>NMR</u>

Indirect determination of H-H distances and a relationship between hydrogen, carbon, nitrogen, and other atoms.

It provides local properties of the structures.

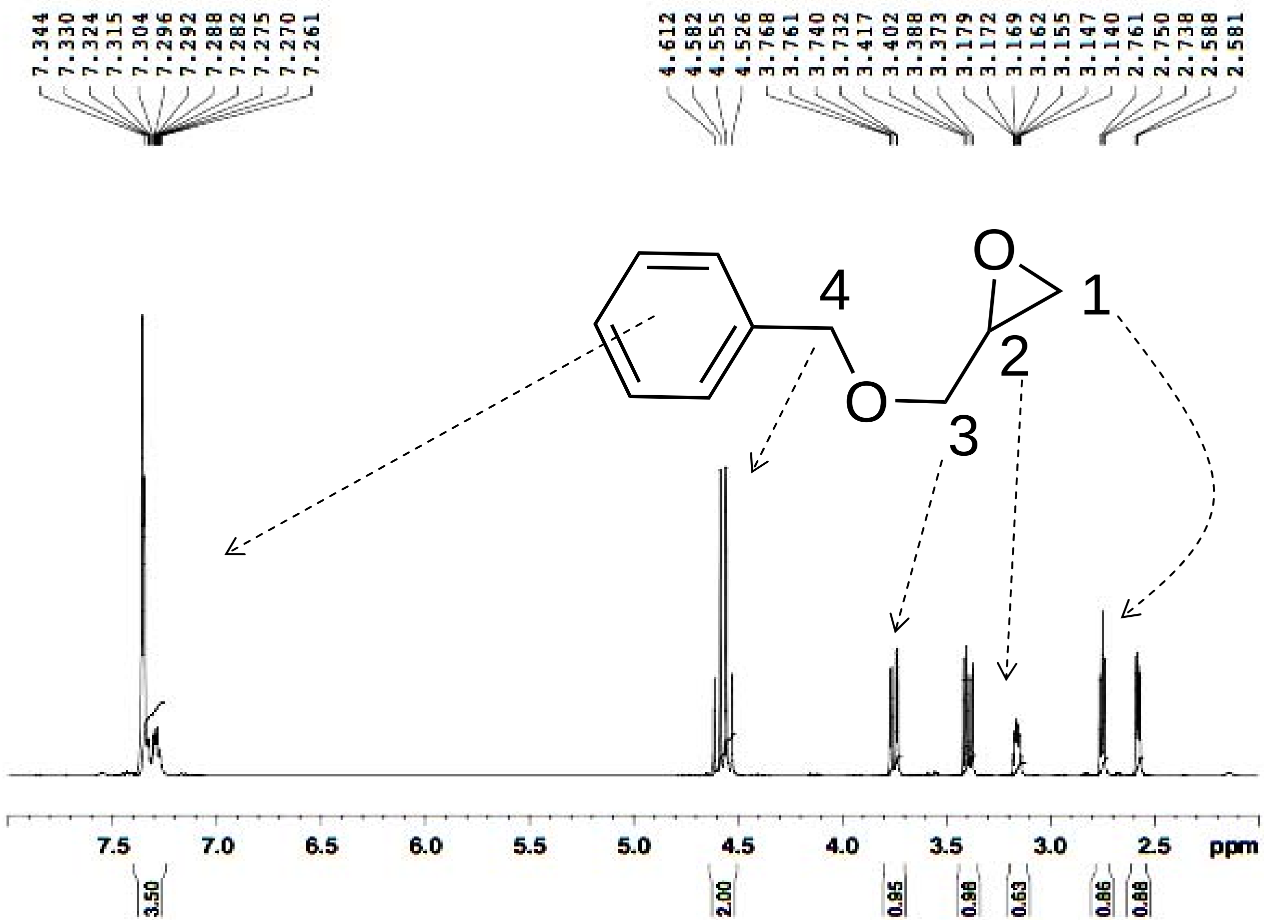
Requires either solution or precipitates.

	Substructural elements	full connectivity	3D structure
X-Ray	(+)	+	+
UV	+	-	-
IR	+	-	-
MS	+	+?	-
NMR	+	+	+

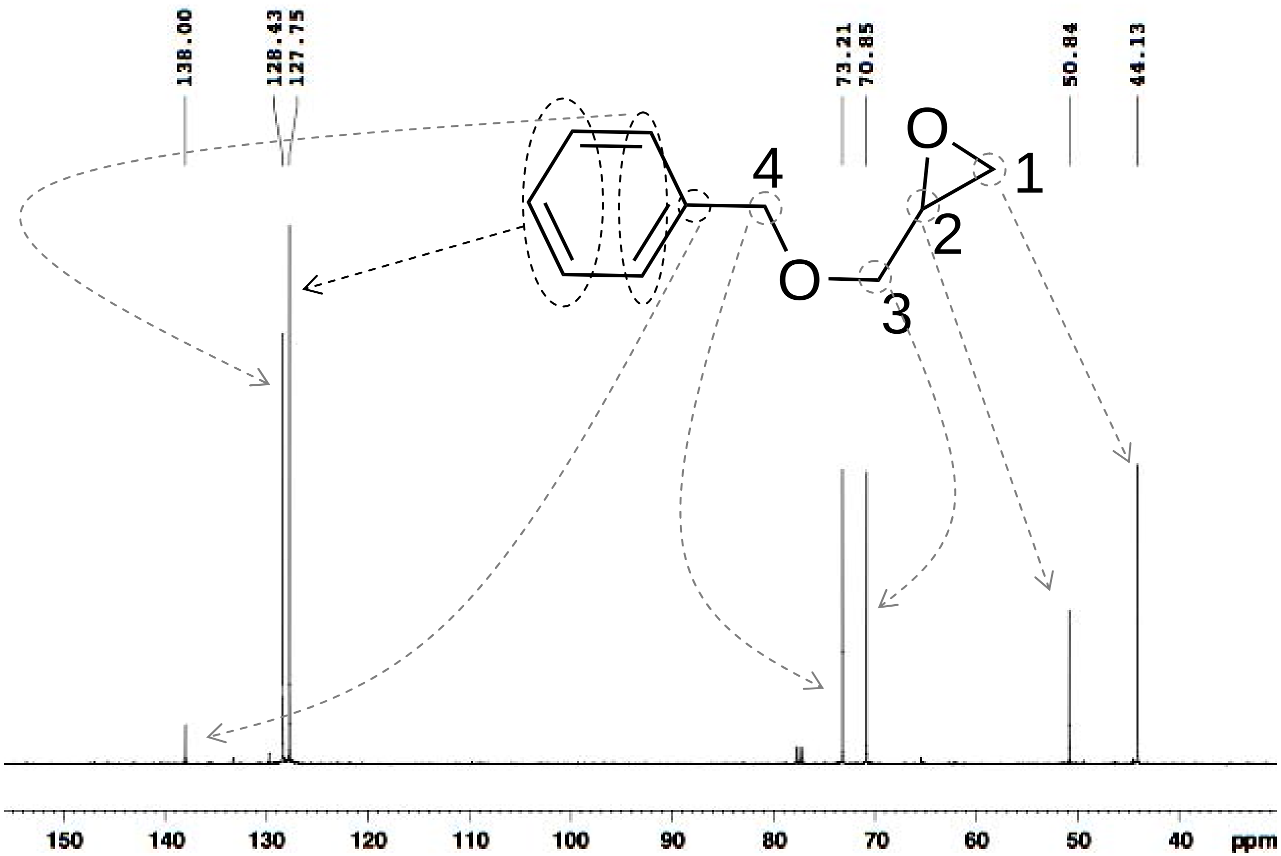
The NMR strategy and the NMR tools:

- number of protons, ^{1}H chemical shifts, ^{1}H-^{1}H couplings ---> ^{1}H spectrum
- number of magnetically nonequivalent carbons ---> ^{13}C spectrum
- number of NMR-detectable other nuclei (^{19}F, ^{31}P, …, ^{15}N?) ---> X spectrum
- ^{1}H-^{13}C direct correlation (one-bond) ---> HSQC, (C,H COSY, HMQC)
- identification of ^{1}H spin systems ---> TOCSY
- ^{1}H coupling network ---> COSY
- ^{1}H-X (X=^{13}C, ^{15}N, ^{19}F, ^{31}P, etc) long-range correlation ---> HMBC(COLOC)
- stereochemistry, 3D structure ---> NOESY, ROESY

Proton (^{1}H) NMR spectrum

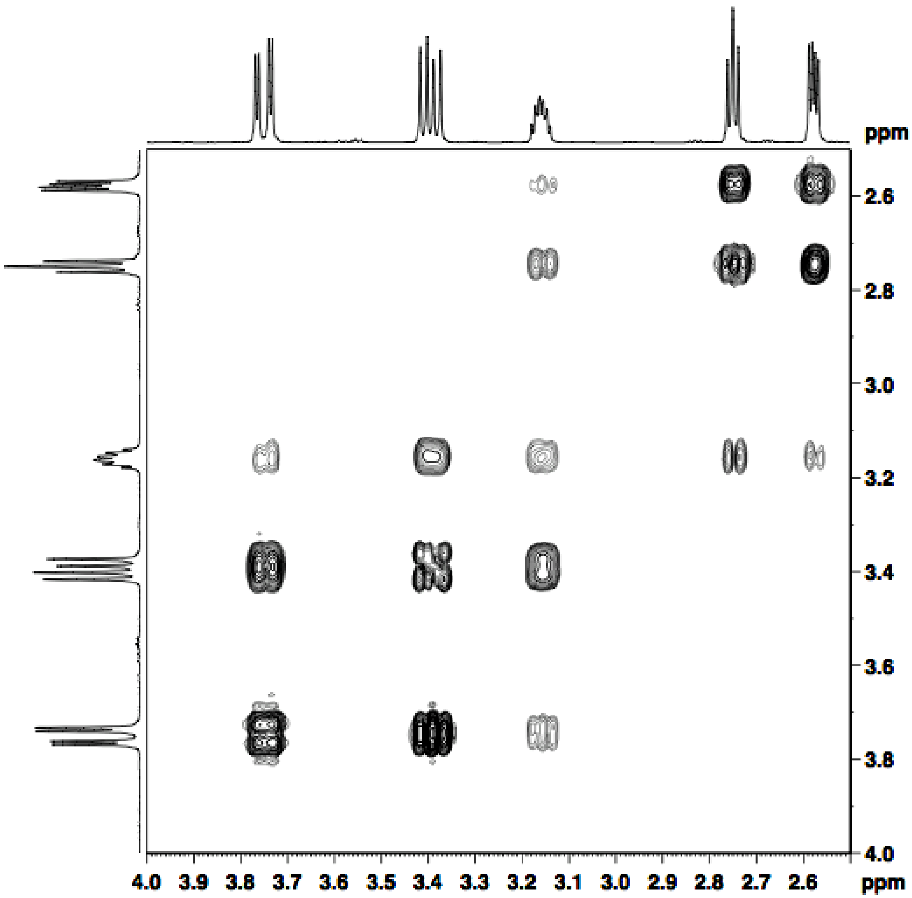


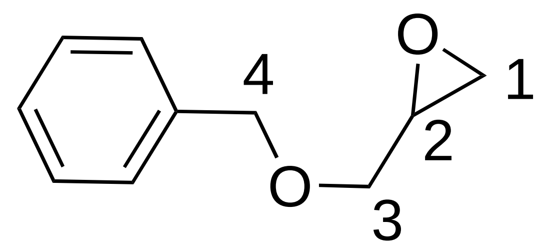
Carbon-13 (^{13}C) NMR spectrum



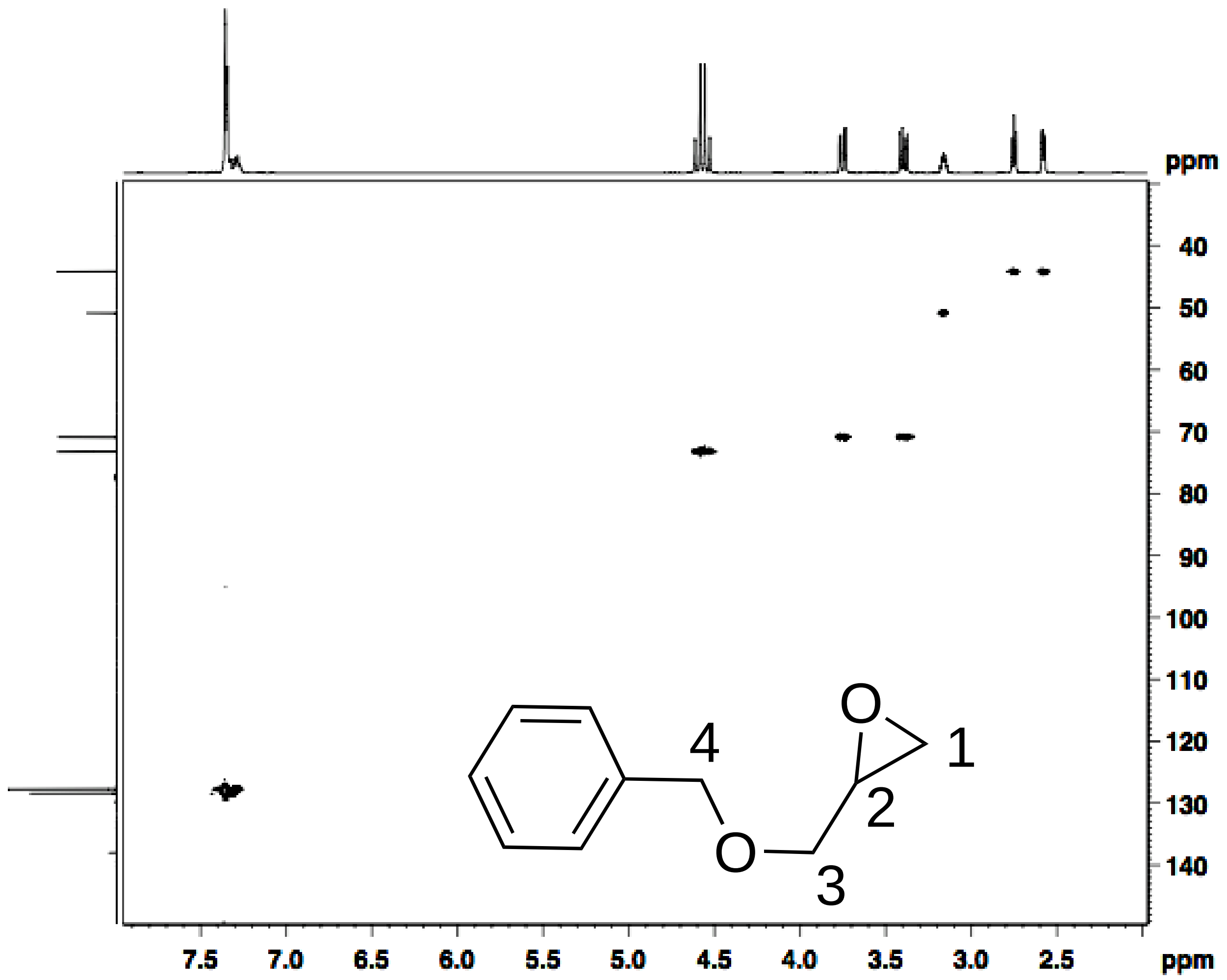
COSY - COrrelation SpectroscopY:

correlates scalarly coupled protons





HMQC - Heteronuclear Multiple Quantum Coherence

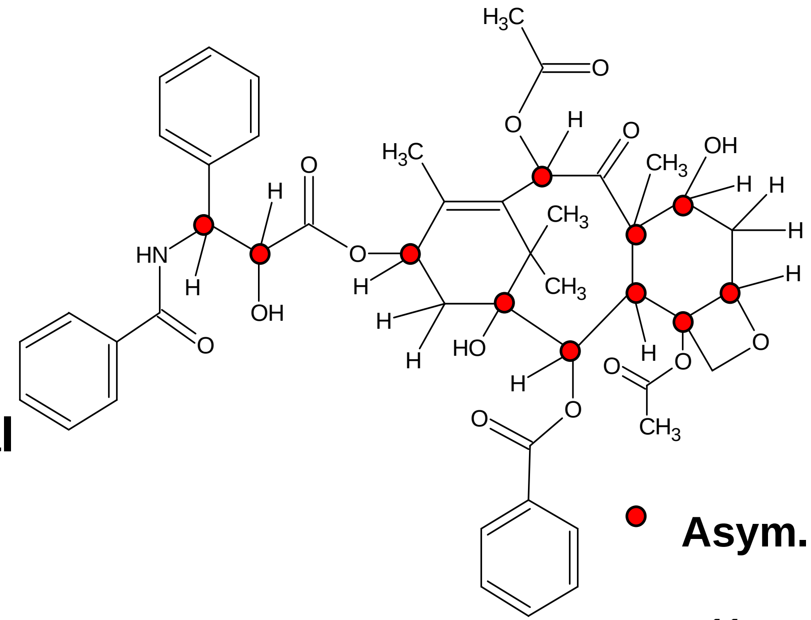


Taxol: **anticancer drug**

(MW: 853.906) (MS)

$C_{47}H_{51}NO_{14}$

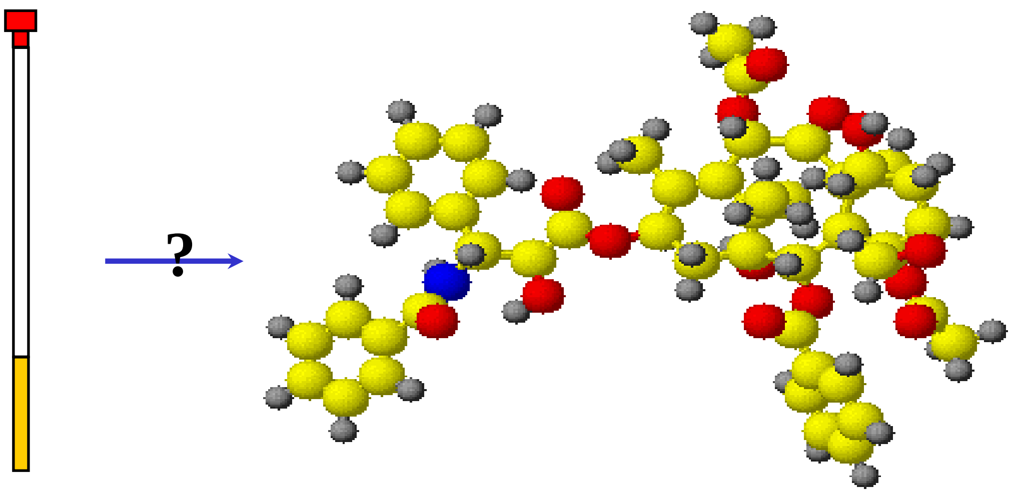
(the number of constitutional isomers >> 10^{30} !!!)



Asym. Carbon (11)

2^{11} = 2048 stereoisomers !!!

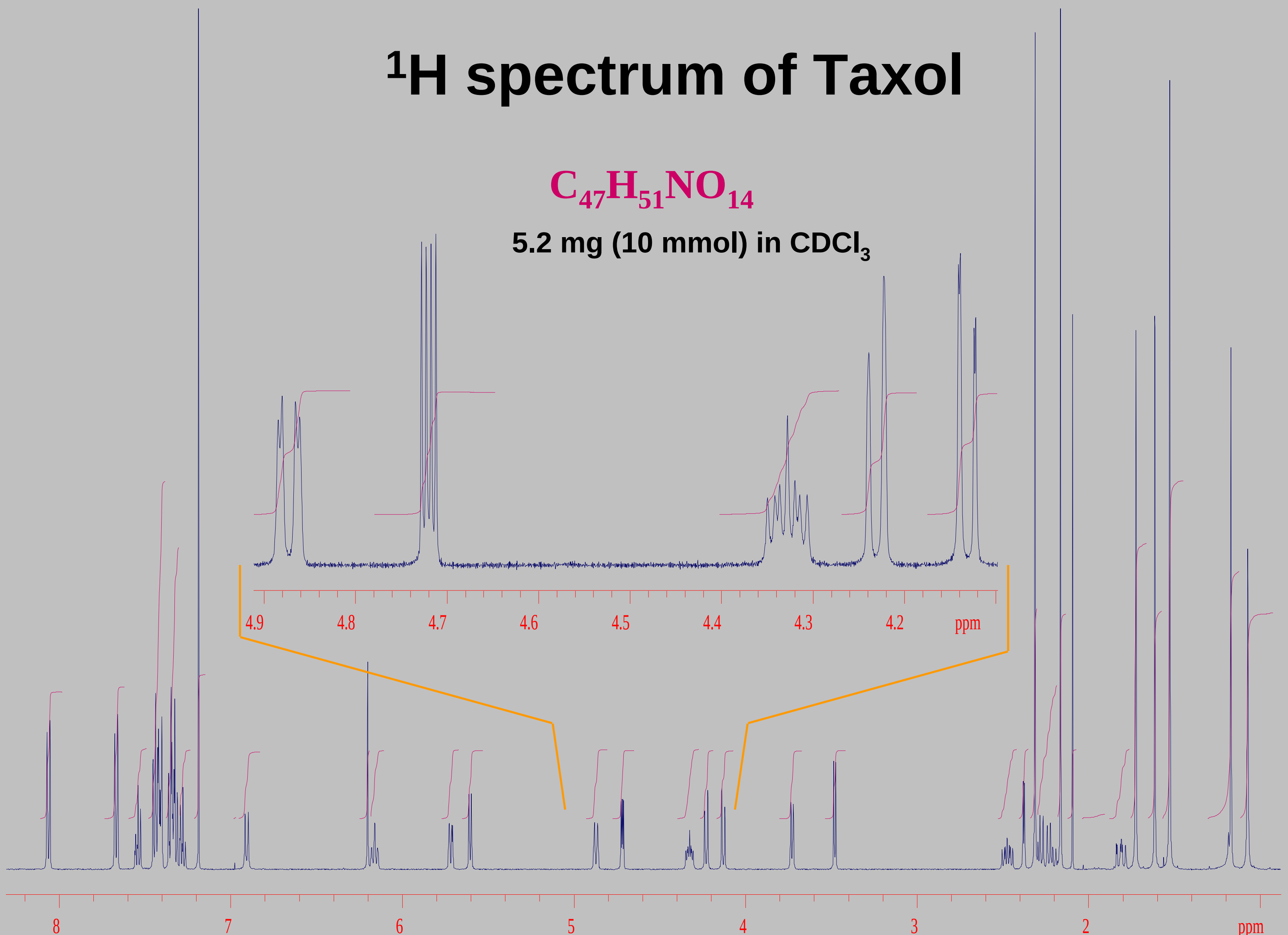
紫杉醇



^{1}H spectrum of Taxol

$C_{47}H_{51}NO_{14}$

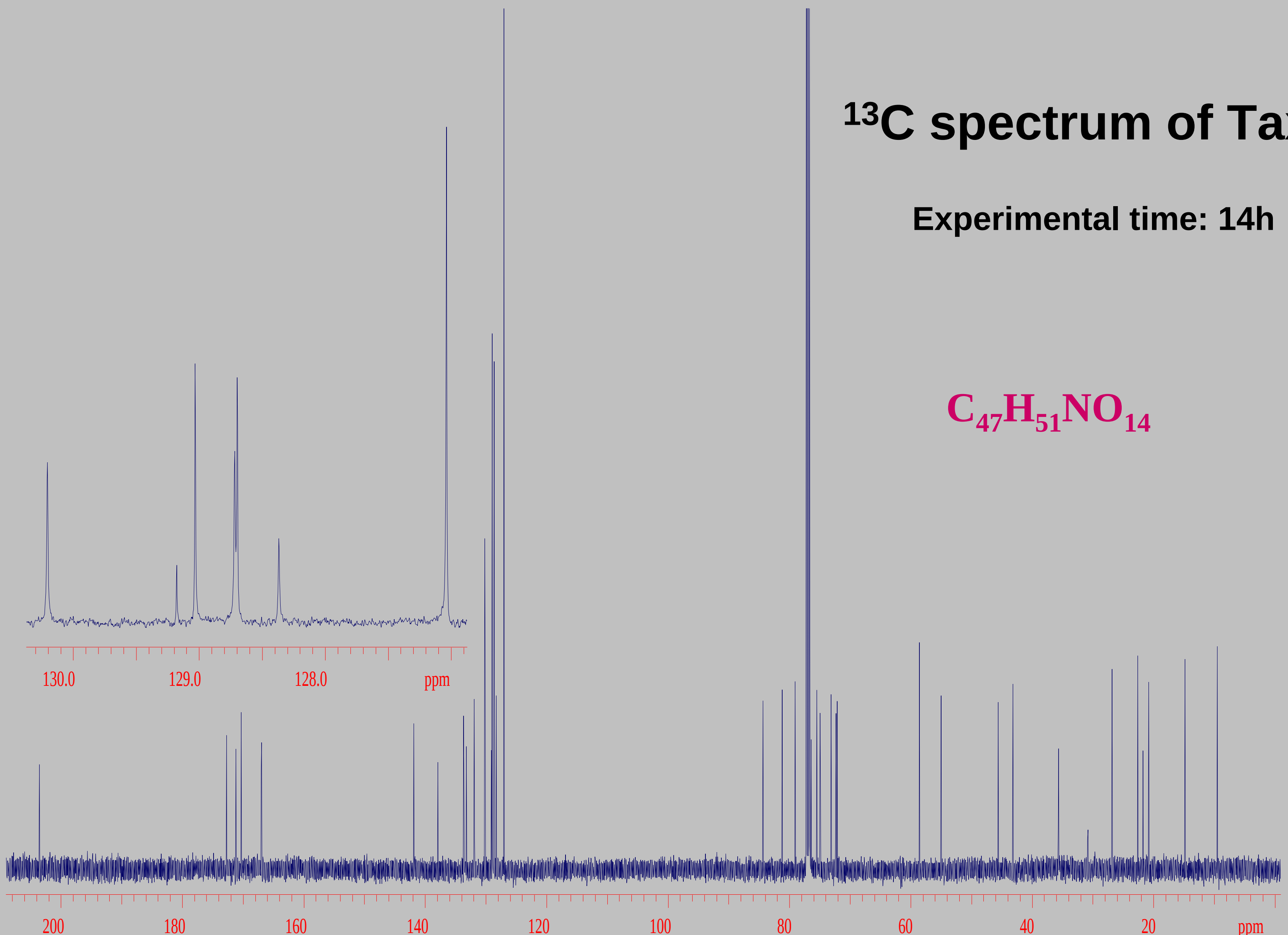
5.2 mg (10 mmol) in $CDCl_3$



^{13}C spectrum of Taxol

Experimental time: 14h

$C_{47}H_{51}NO_{14}$



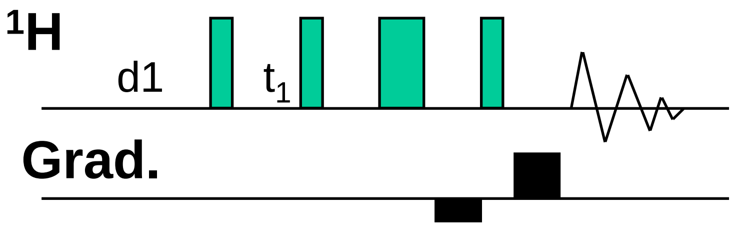
^{1}H shifts (int)		^{13}C shifts (int)	
8.06 (2)	3.48 (1)	203.61	84.41
7.67 (2)	2.47 (1)	172.72	81.19
7.54 (1)	2.38 (1)	171.22	79.05
7.44 (2)	2.31 (3)	170.35	76.52
7.43 (1)	2.29 (1)	167.04	75.57
7.41 (2)	2.22 (1)	167.01	74.98
7.35 (2)	2.17 (3)	141.95	73.20
7.33 (2)	2.10 (imp.)	137.99	72.41
7.28 (1)	1.81 (1)	133.71	72.18
6.91 (1)	1.73 (1)	133.65	58.65
6.21 (1)	1.72 (3)	133.23	55.04
6.16 (1)	1.62 (3)	131.97	45.64
5.72 (1)	1.53 (H_2O)	130.21 (2)	43.19
5.61 (1)	1.17 (3)	129.18	35.72
4.87 (1)	1.08 (3)	129.03 (2)	35.63
4.72 (1)		128.72 (2)	26.88
4.33 (1)		128.70 (2)	22.63
4.23 (1)		128.37	21.83
4.13 (1)		127.04 (2)	20.84
3.73 (1)		127.04 (2)	14.83
			9.57

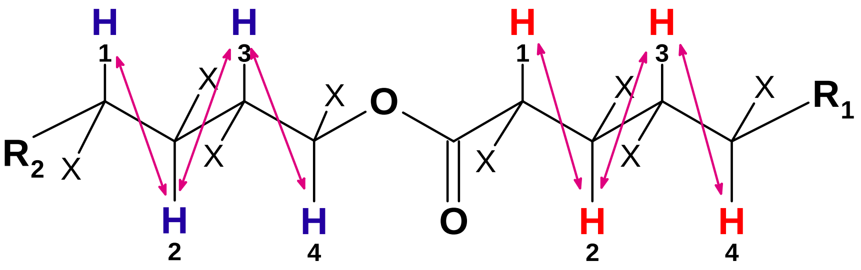
51 protons | **47 carbons**

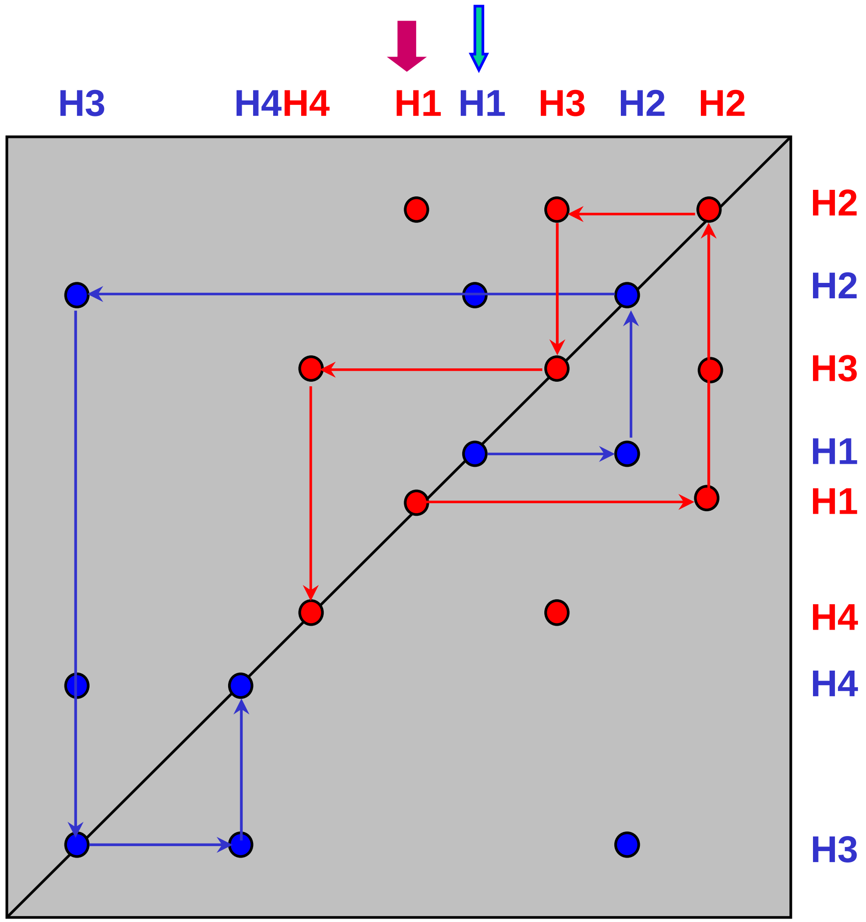
COSY - COrrelation SpectroscopY

(correlates scalarly coupled protons)

The gradient DQF-COSY sequence:

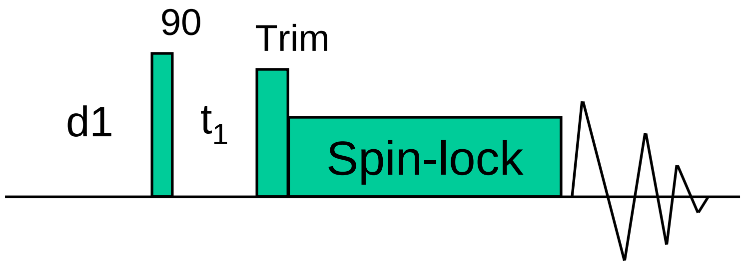


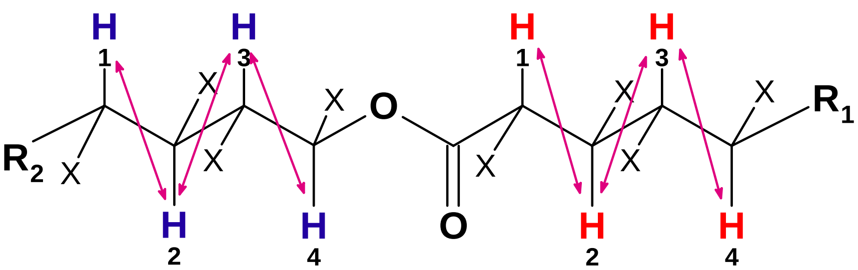


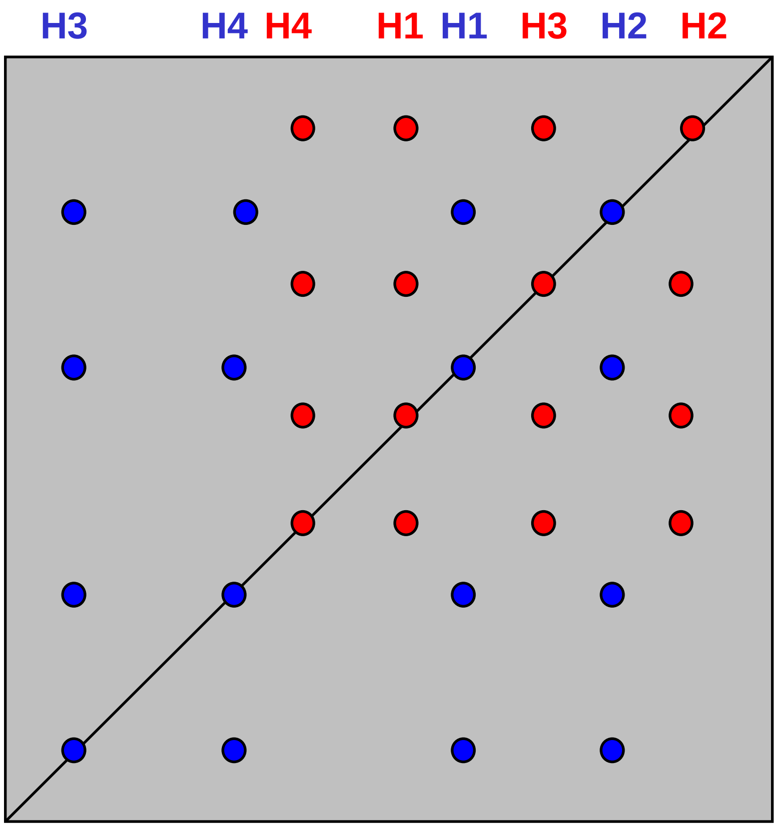


TOCSY - TOtal Correlation SpectroscopY

(identifies protons belonging to the same scalar coupling network)

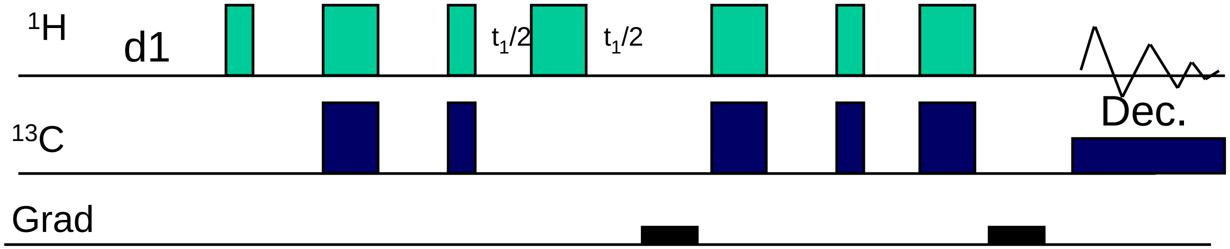


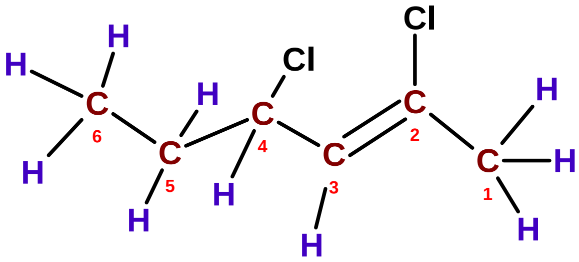


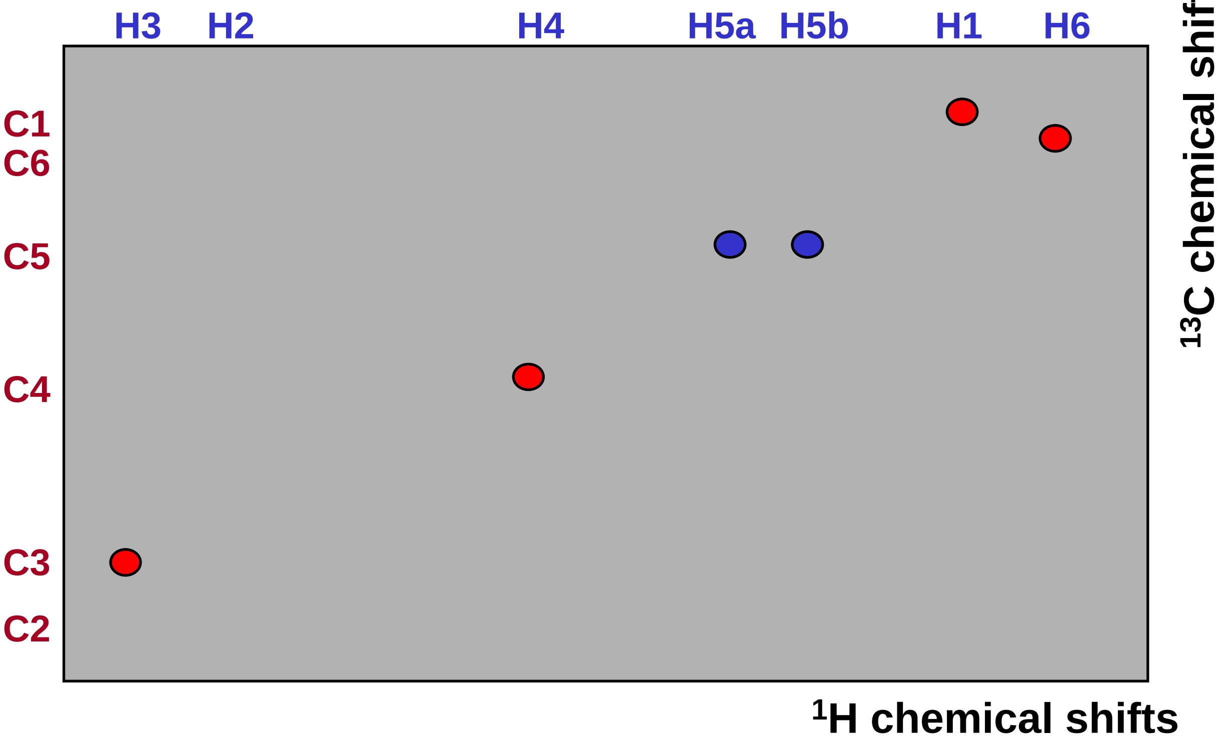


HSQC - Heteronuclear Single Quantum Coherence

(correlates X-^{1}H chemical shifts via one-bond ^{1}J(XH) couplings)







Results from the HSQC experiment:

Proton-Carbon Pairs

¹H (nH)	¹³C	¹H (nH)	¹³C
8.06 (2)	130.21 (d*)	4.72 (1)	73.20 (d)
7.67 (2)	127.04 (d*)	4.33 (1)	72.18 (d)
7.54 (1)	133.71 (d)	4.23 (1); 4.13 (1)	76.52 (t)
7.44 (2)	128.70 (d*)	3.73 (1)	45.64 (d)
7.42 (1)	131.97 (d)	3.48 (1)	
7.41 (2)	127.04 (d*)	2.47 (1); 1.81 (1)	35.63 (t)
7.35 (2)	129.03 (d*)	2.38 (1)	
7.33 (2)	128.72 (d*)	2.31 (3)	22.63 (q)
7.28 (1)	128.37 (d)	2.29 (1); 2.22 (1)	35.72 (t)
6.91 (1)		2.17 (3)	20.84 (q)
6.21 (1)	75.57 (d)	1.73 (1)	
6.16 (1)	72.41 (d)	1.72 (3)	14.83 (q)
5.72 (1)	55.04 (d)	1.62 (3)	9.57 (q)
5.61 (1)	74.98 (d)	1.17 (3)	26.88 (q)
4.87 (1)	84.41 (d)	1.08 (3)	21.83 (q)

Quaternery Carbons

203.61 (s)
172.72 (s)
171.22 (s)
170.35 (s)
167.04 (s)
167.01 (s)
141.95 (s)
137.99 (s)
133.65 (s)
133.23 (s)
129.18 (s)
81.19 (s)
79.05 (s)
58.65 (s)
43.19 (s)

Conclusions:

a, cross-peaks identify C-H pairs

b, no cross-peak at a ^{1}H chemical shift: exchangable proton

c, no cross-peat at a ^{13}C chemical shift: quaternary carbon

We have:

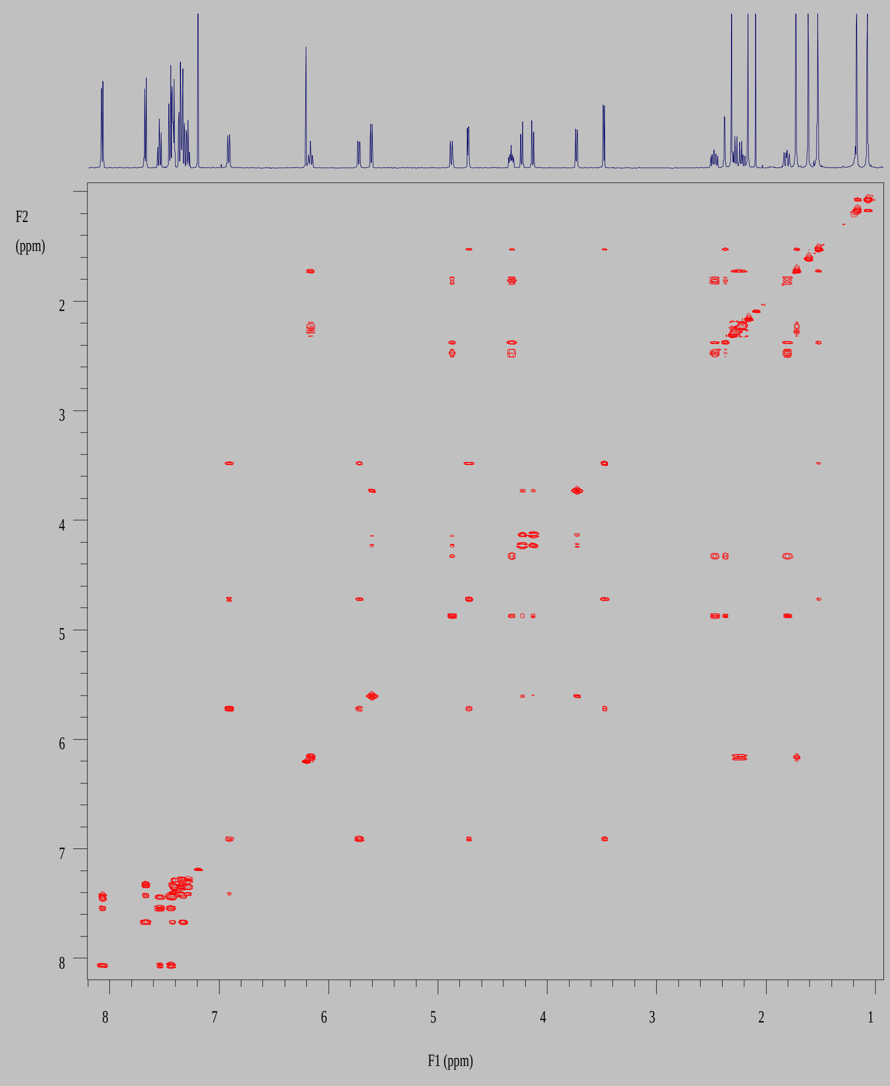
15 quaternary

17 + 6* CH

3 CH_2

6 CH_3 carbons

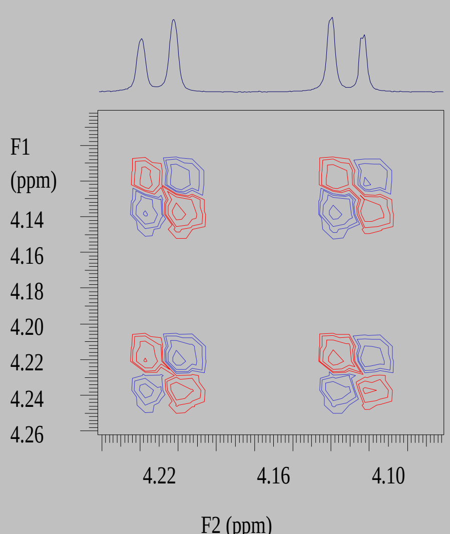
TOCSY spectrum of Taxol

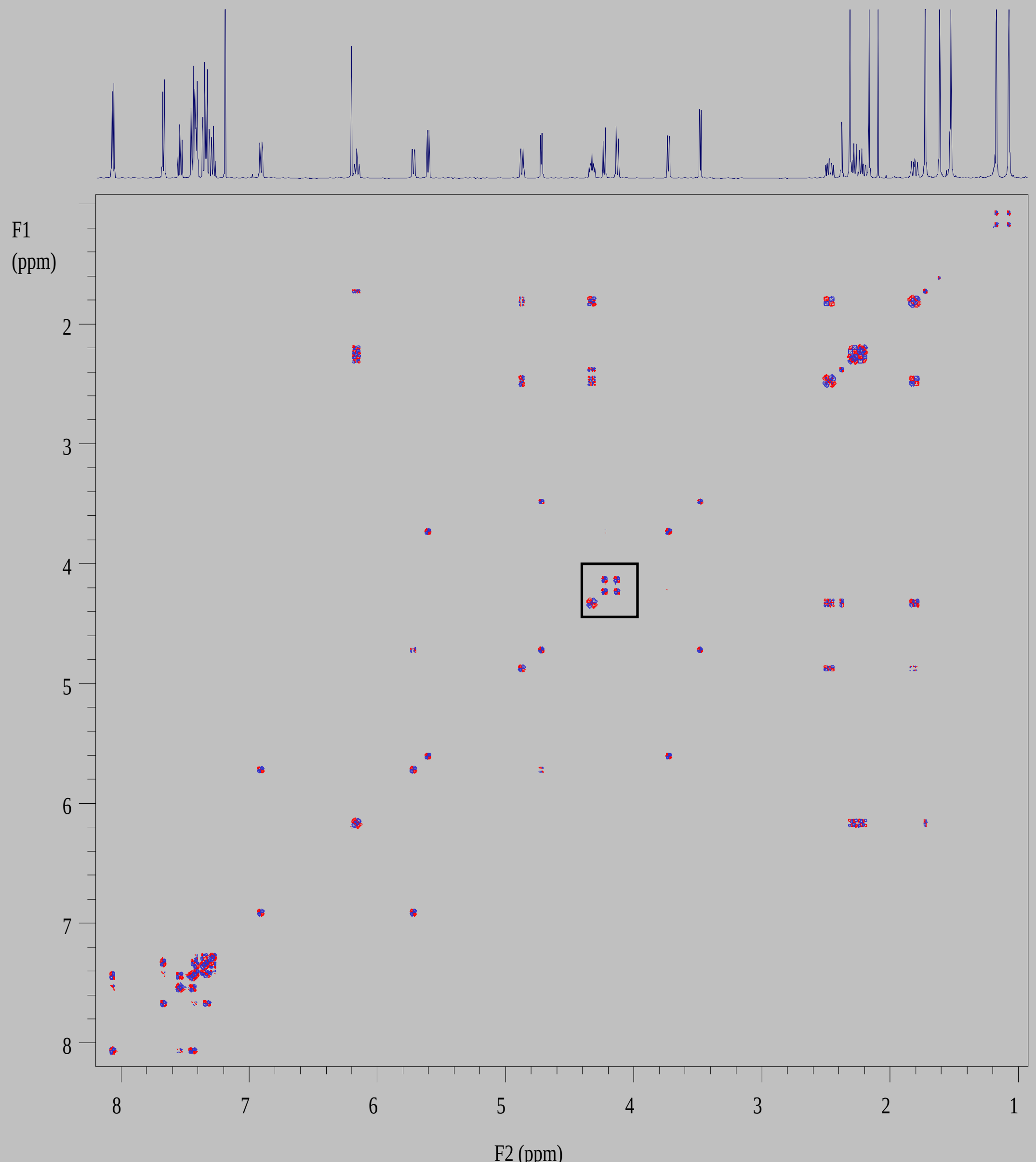


nt=2 per increment
256 complex points in F1
mixing time = 160 msec
exp. time=32 min

DQF-COSY of Taxol

nt=1 per increment
ni=640, phase=1,2
exp. time=40 min



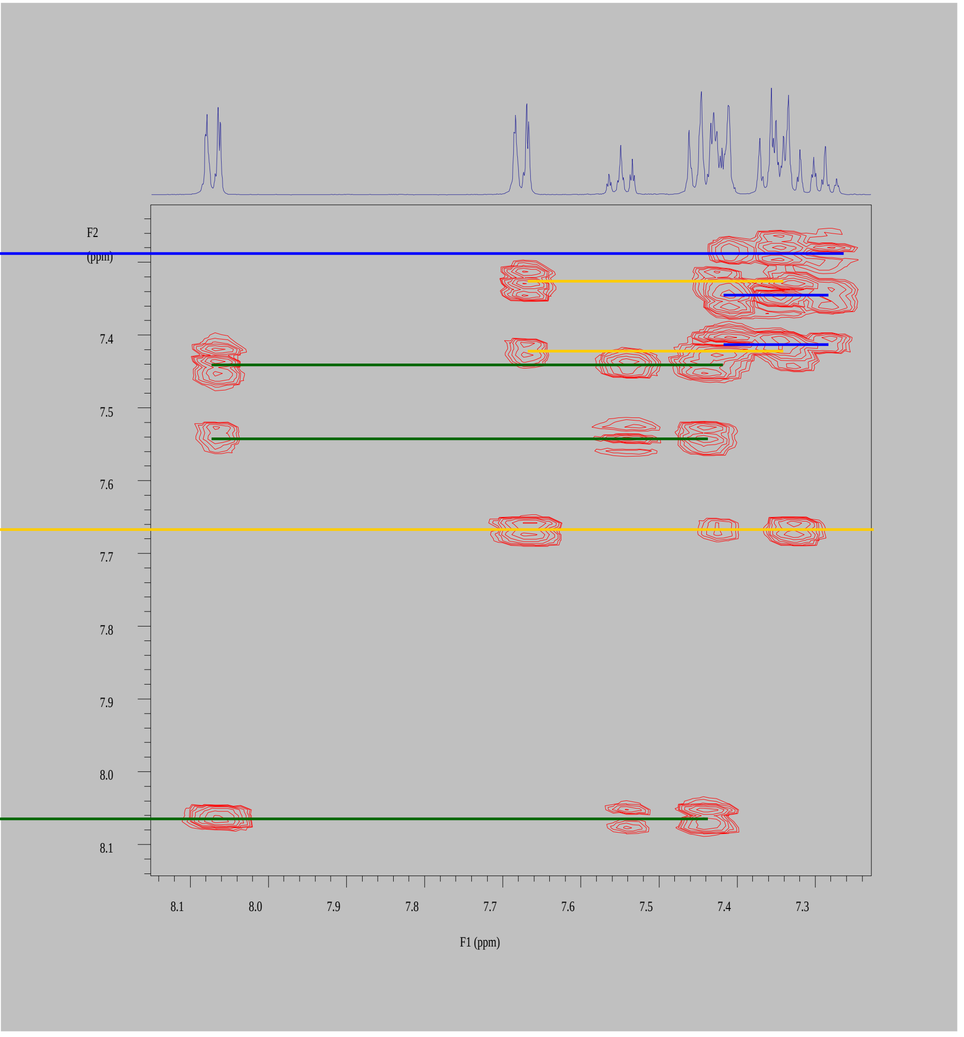


^{1}H TOCSY spectrum of Taxol (expansion #1)

B: 7.41, 7.35, 7.28

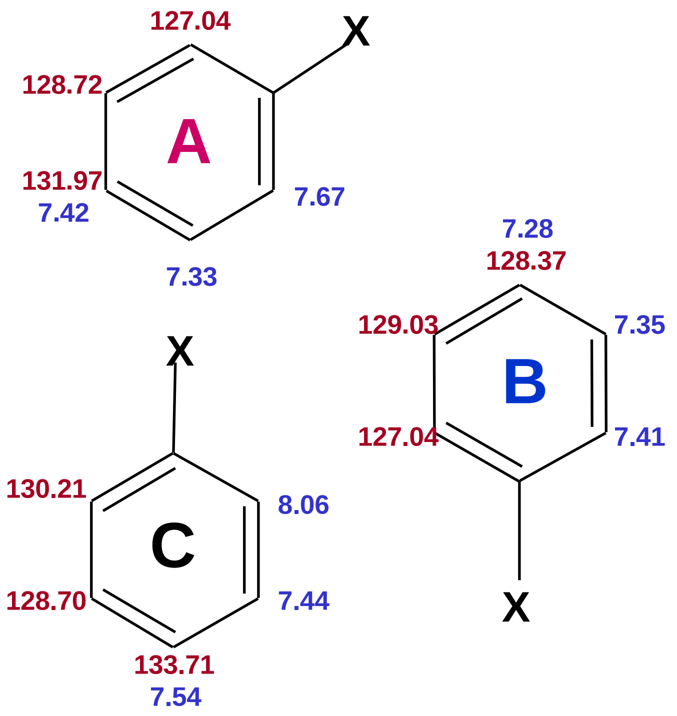
A: 7.67, 7.43, 7.33

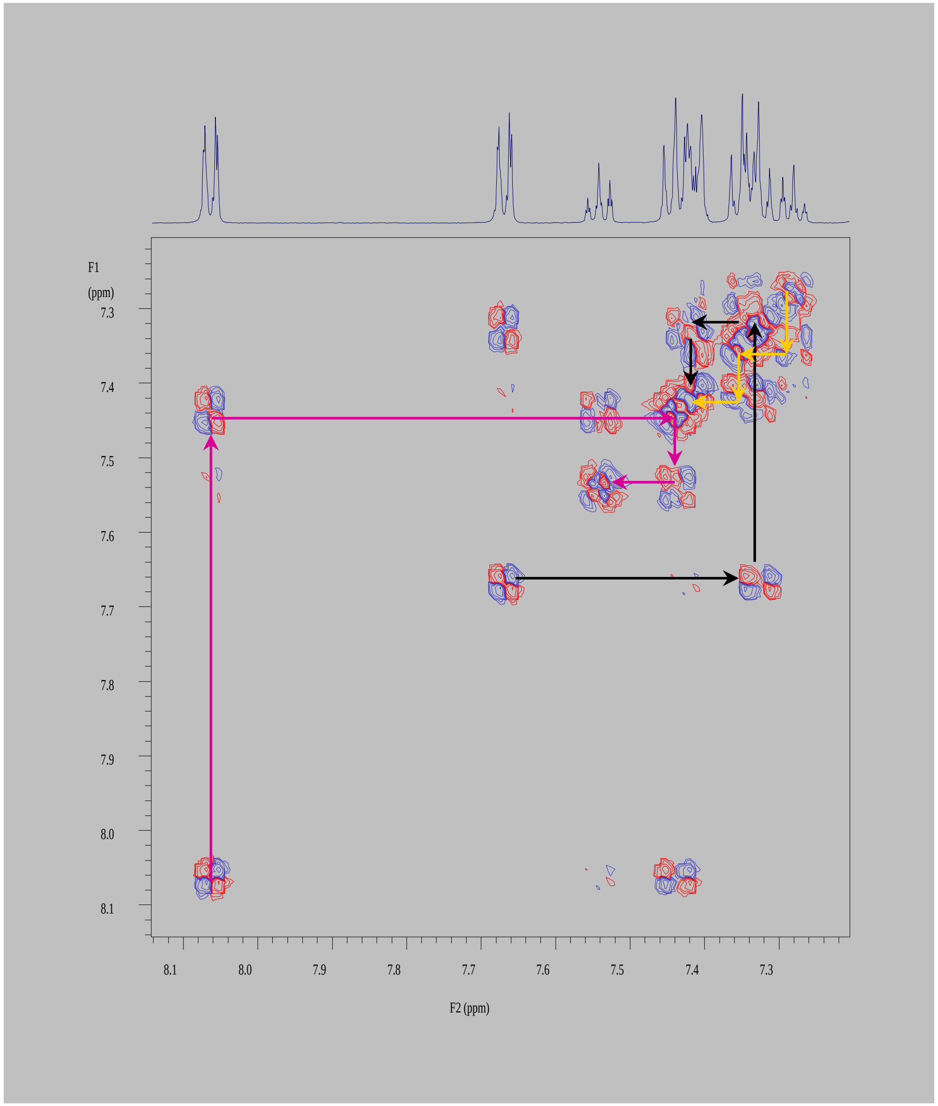
C: 8.06, 7.54, 7.44



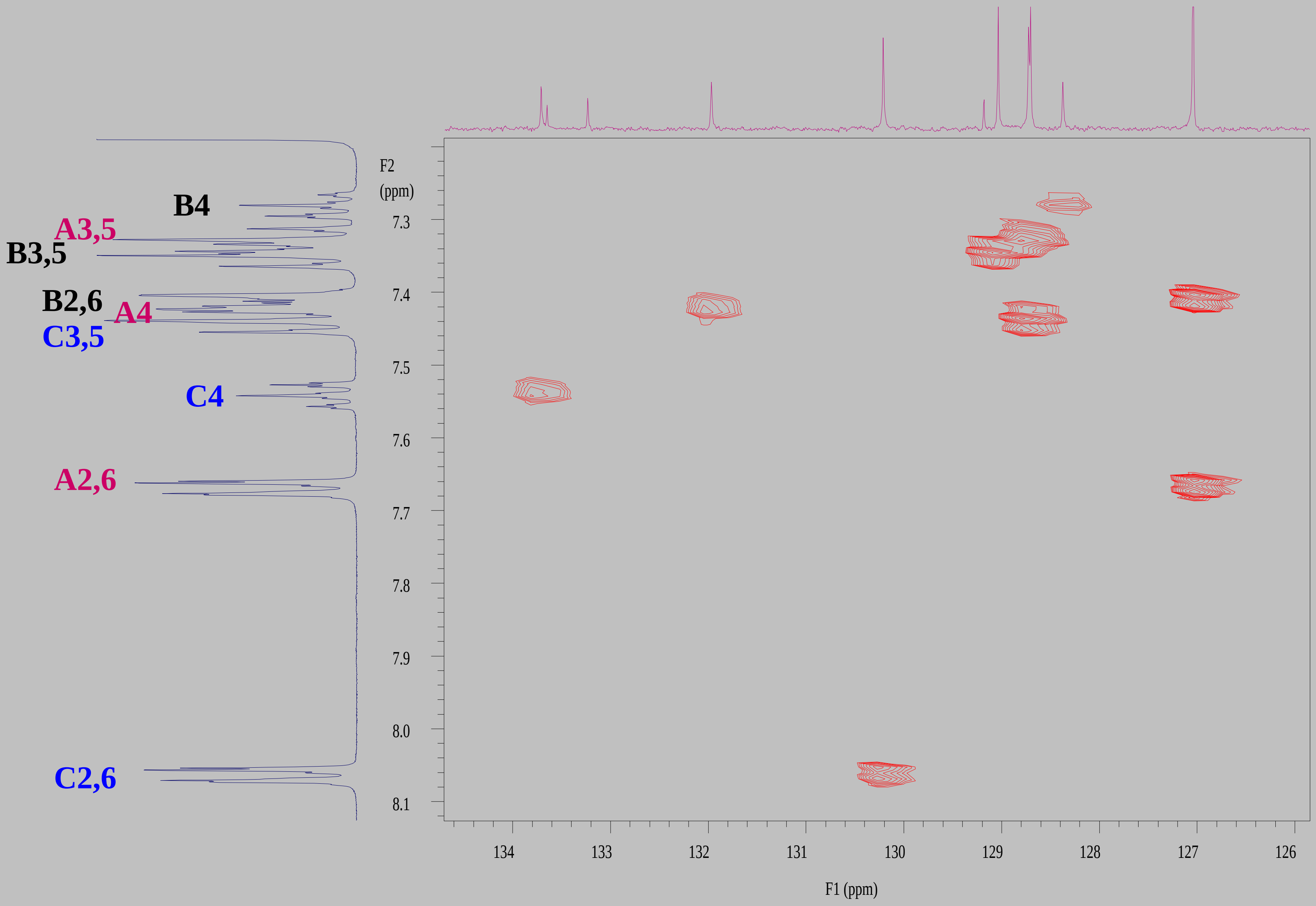
DQF-COSY of Taxol
(expansion #1)

Known from TOCSY:
8.06, 7.54, 7,44
7.67, 7.42, 7.33
7.41, 7.35, 7.28



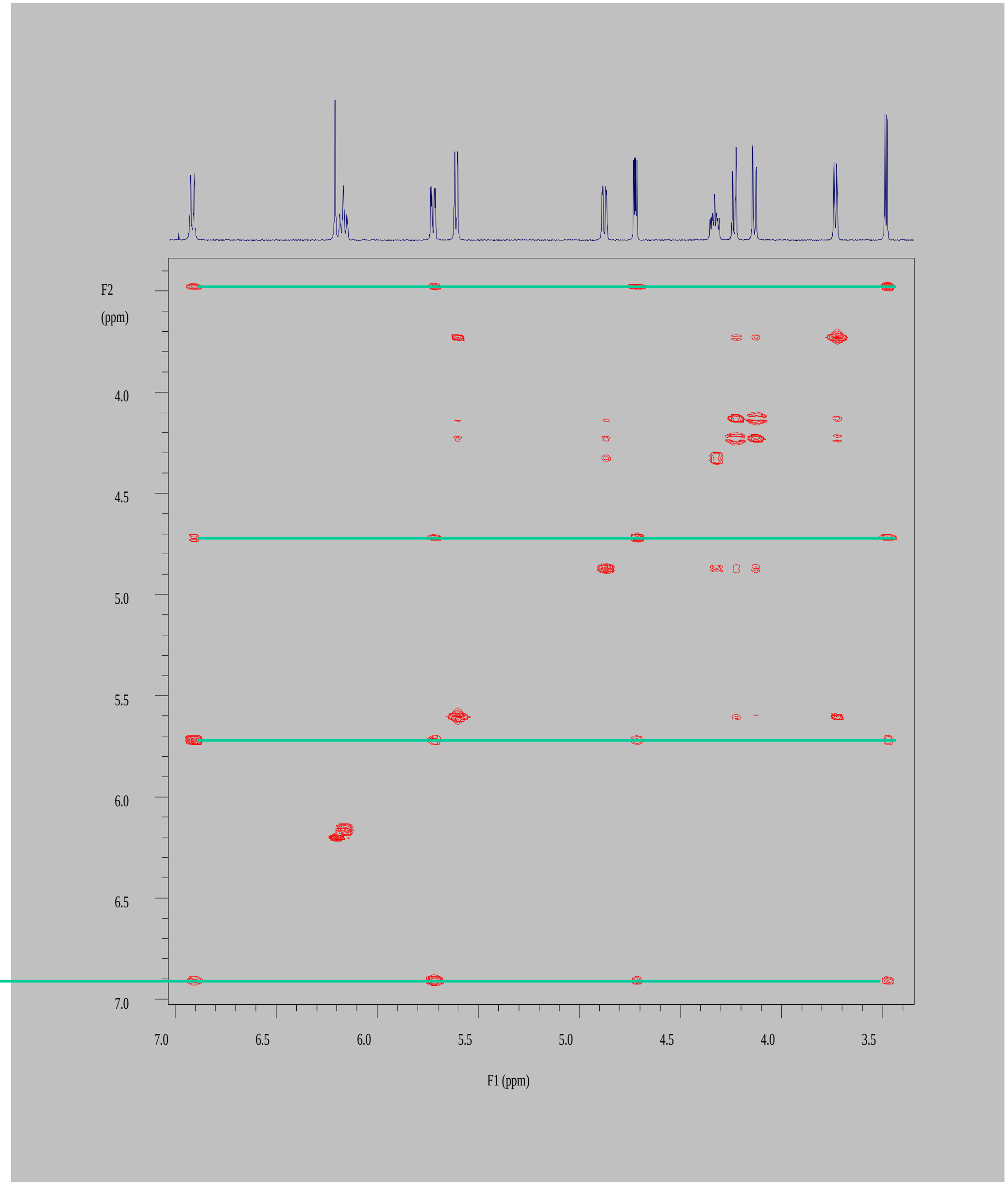


Gradient HSQC spectrum of Taxol (expansion #1)



[1]H TOCSY spectrum of Taxol

(expansion #2)



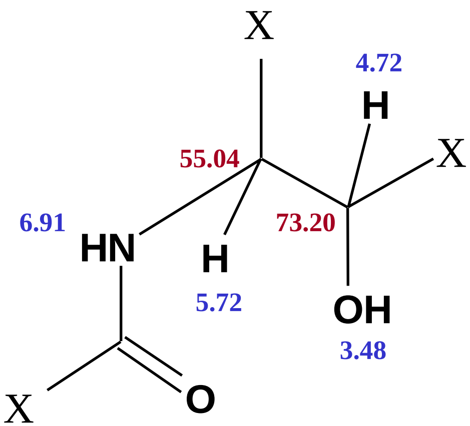
6.91, 5.72, 4.72, 3.48

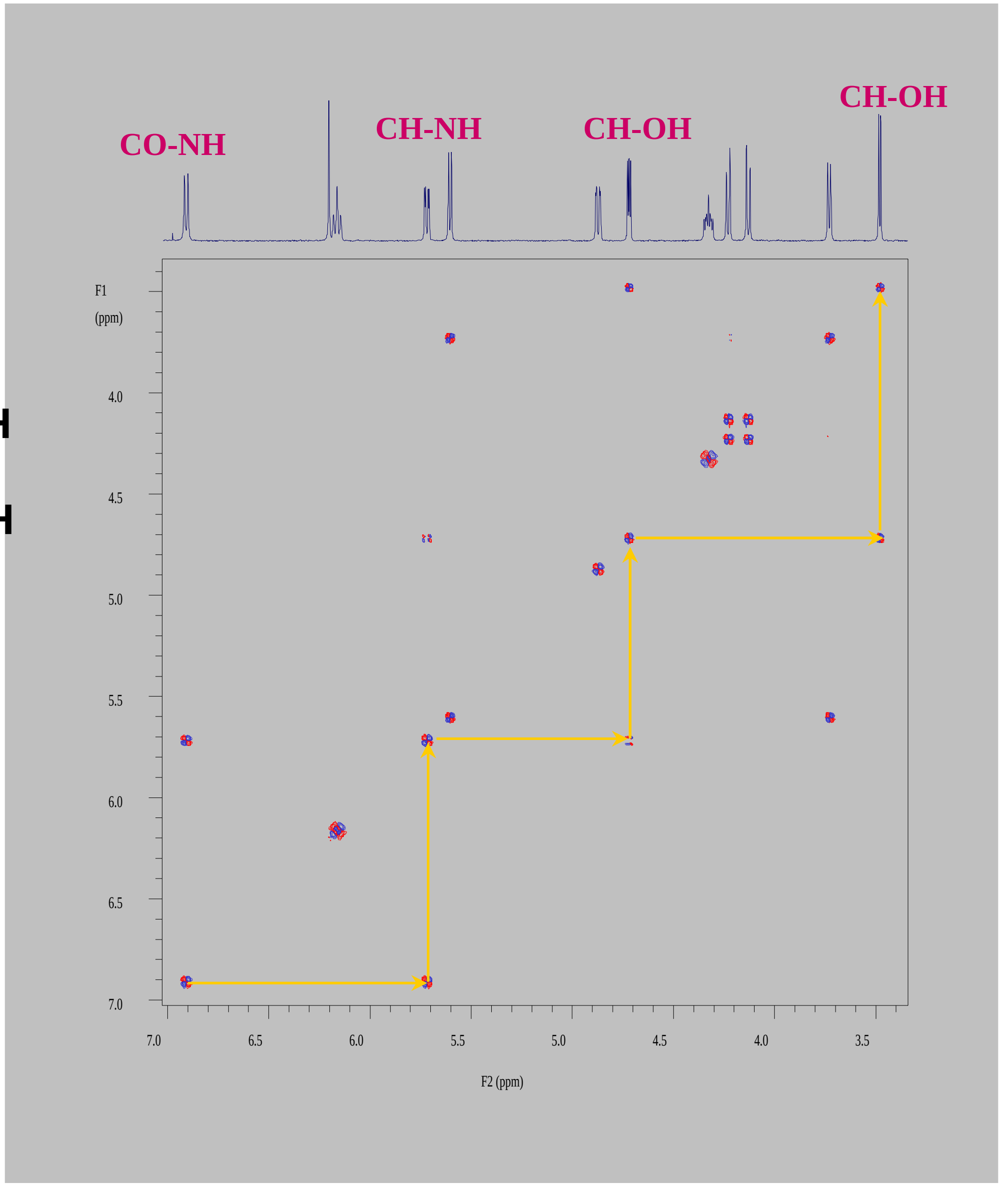
DQF-COSY of Taxol
(expansion #2)

Known from TOCSY:
6.91, 5.72, 4.72 3.48

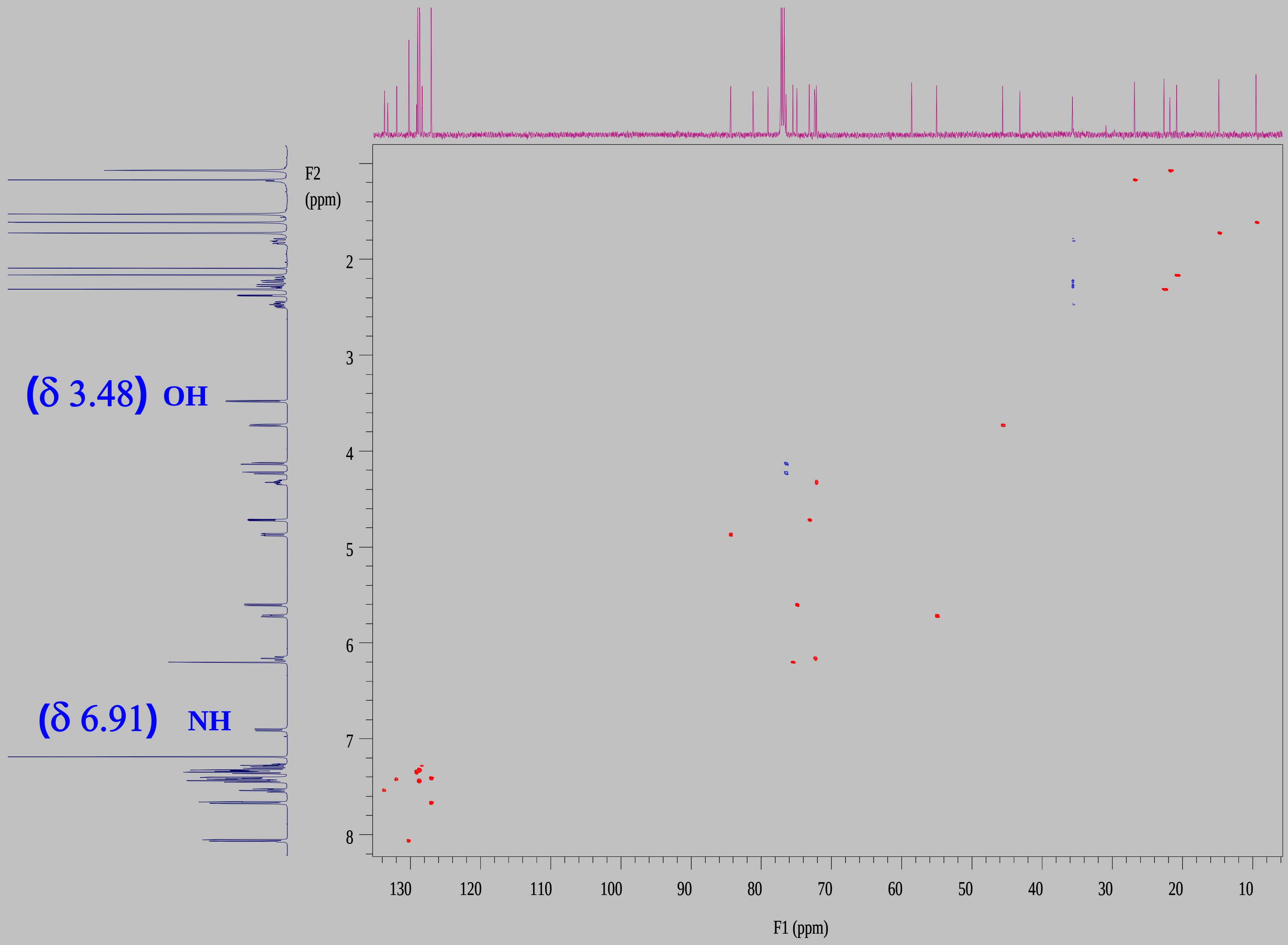
Known from ^{15}N-HSQC: 6.91 is NH

Known from ^{13}C-HSQC: 3.48 is OH

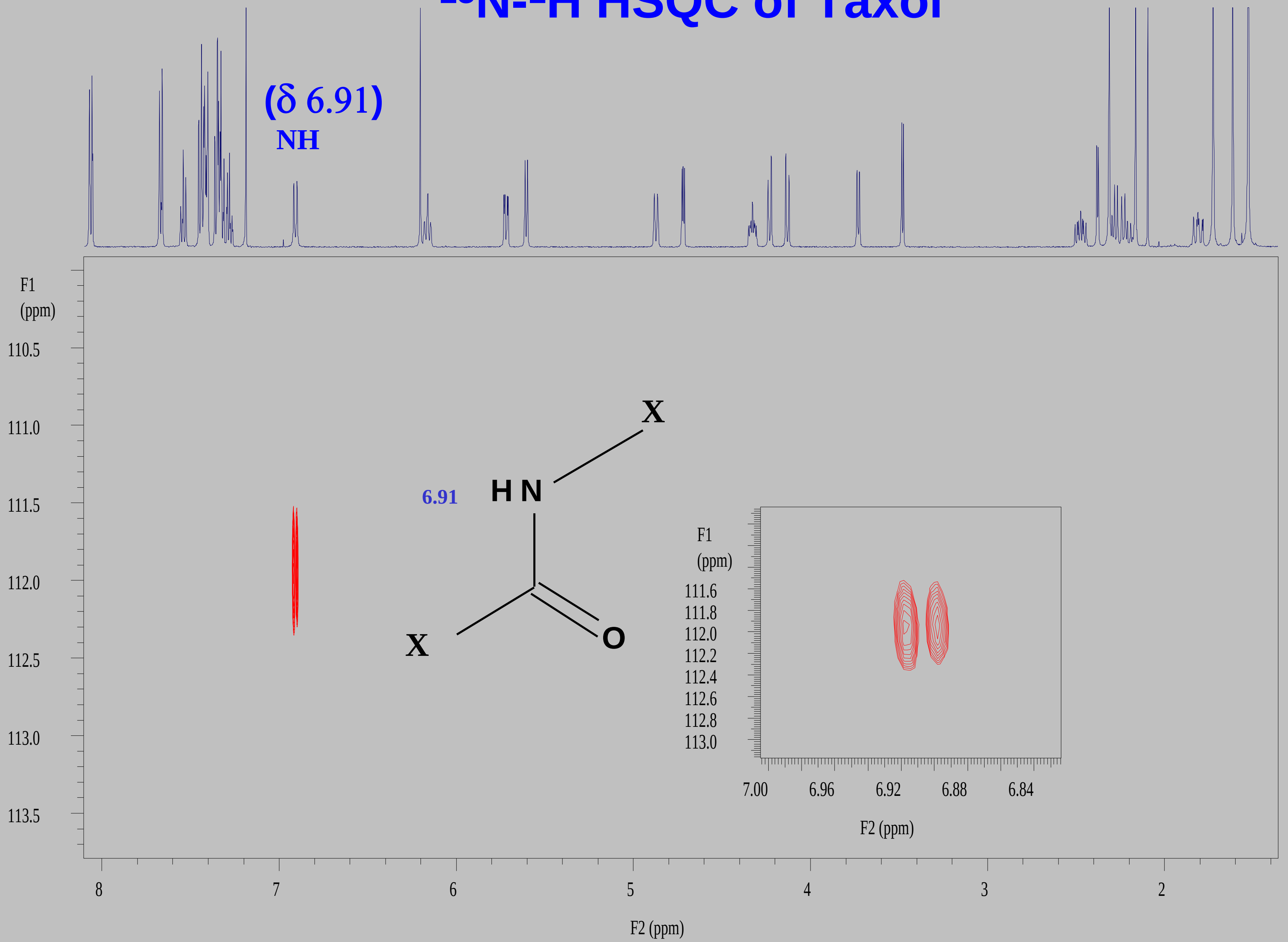




Gradient HSQC spectrum of Taxol

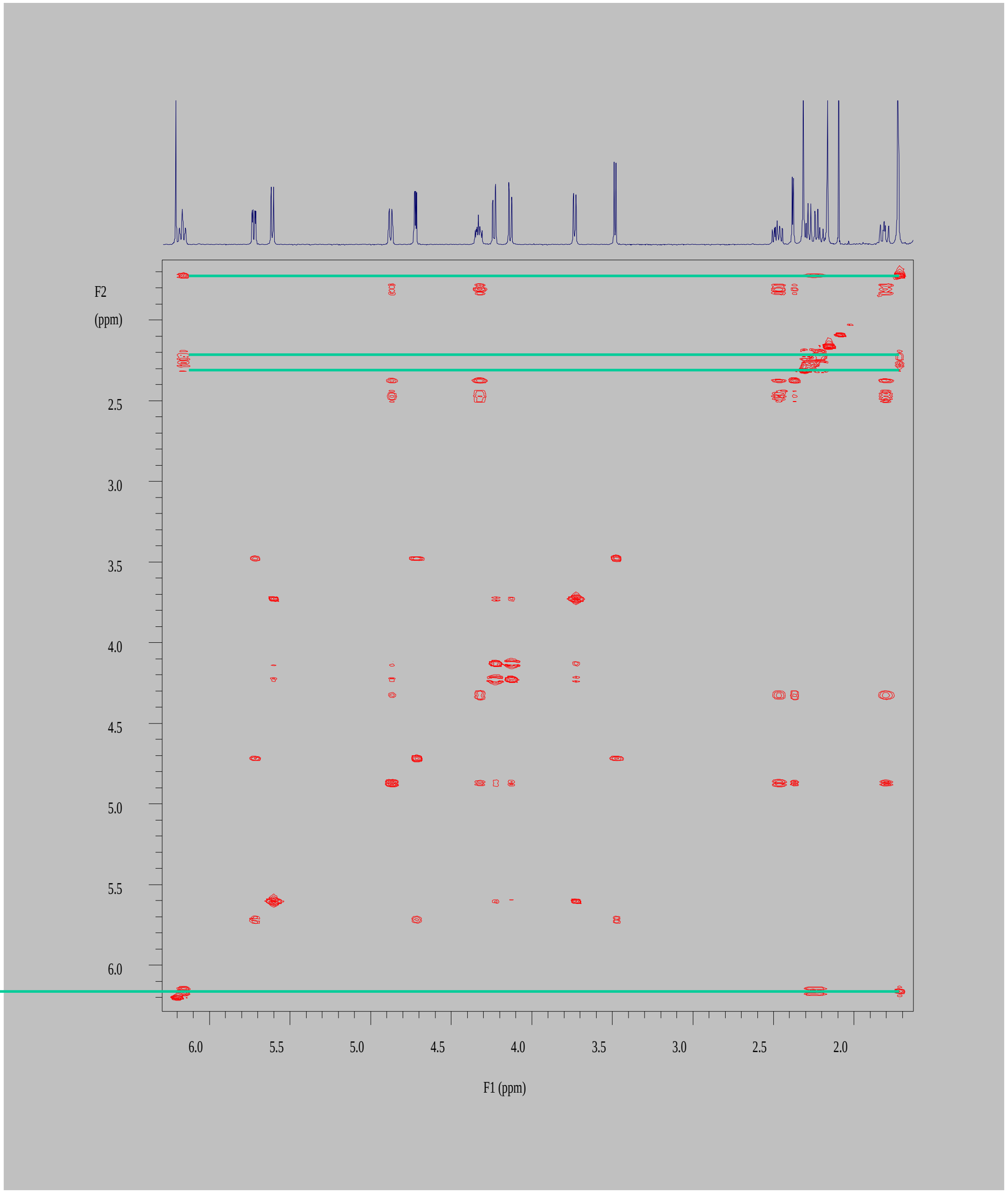


^{15}N-^{1}H HSQC of Taxol



[1]H TOCSY spectrum of Taxol

(expansion #3)

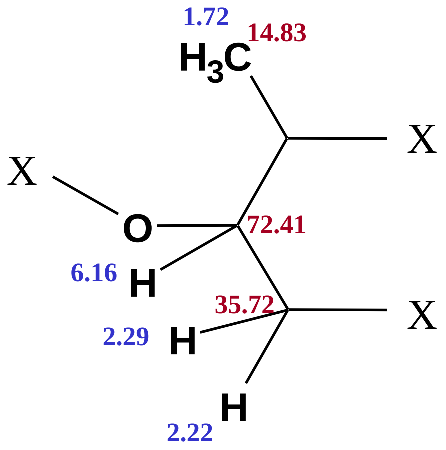


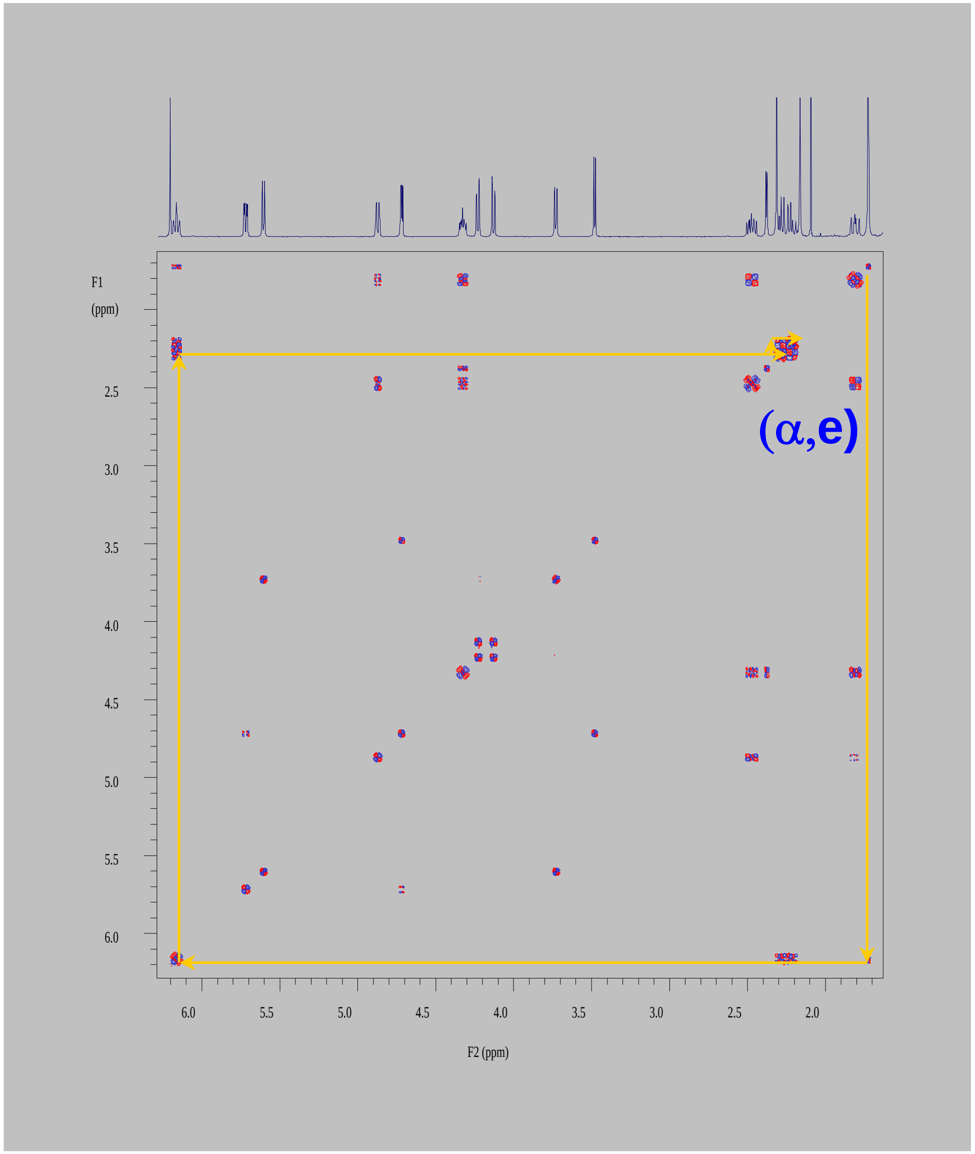
6.16, 2.29, 2.22, 1.72

DQF-COSY of Taxol
(expansion #3)

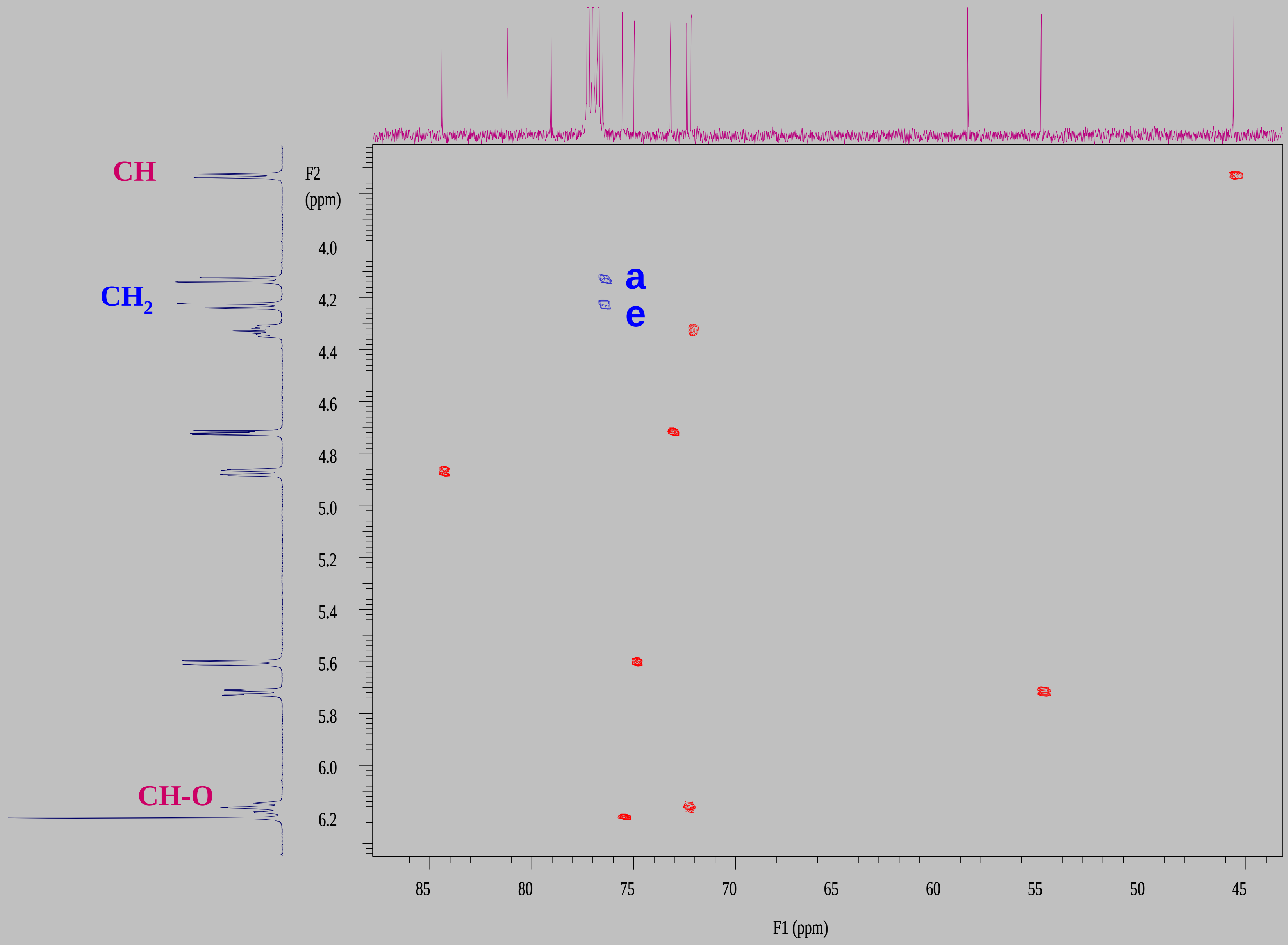
Known from TOCSY:
6.16, 2.29, 2,22, 1.72

Known from HSQC:
2.29, 2.22 are geminal partners

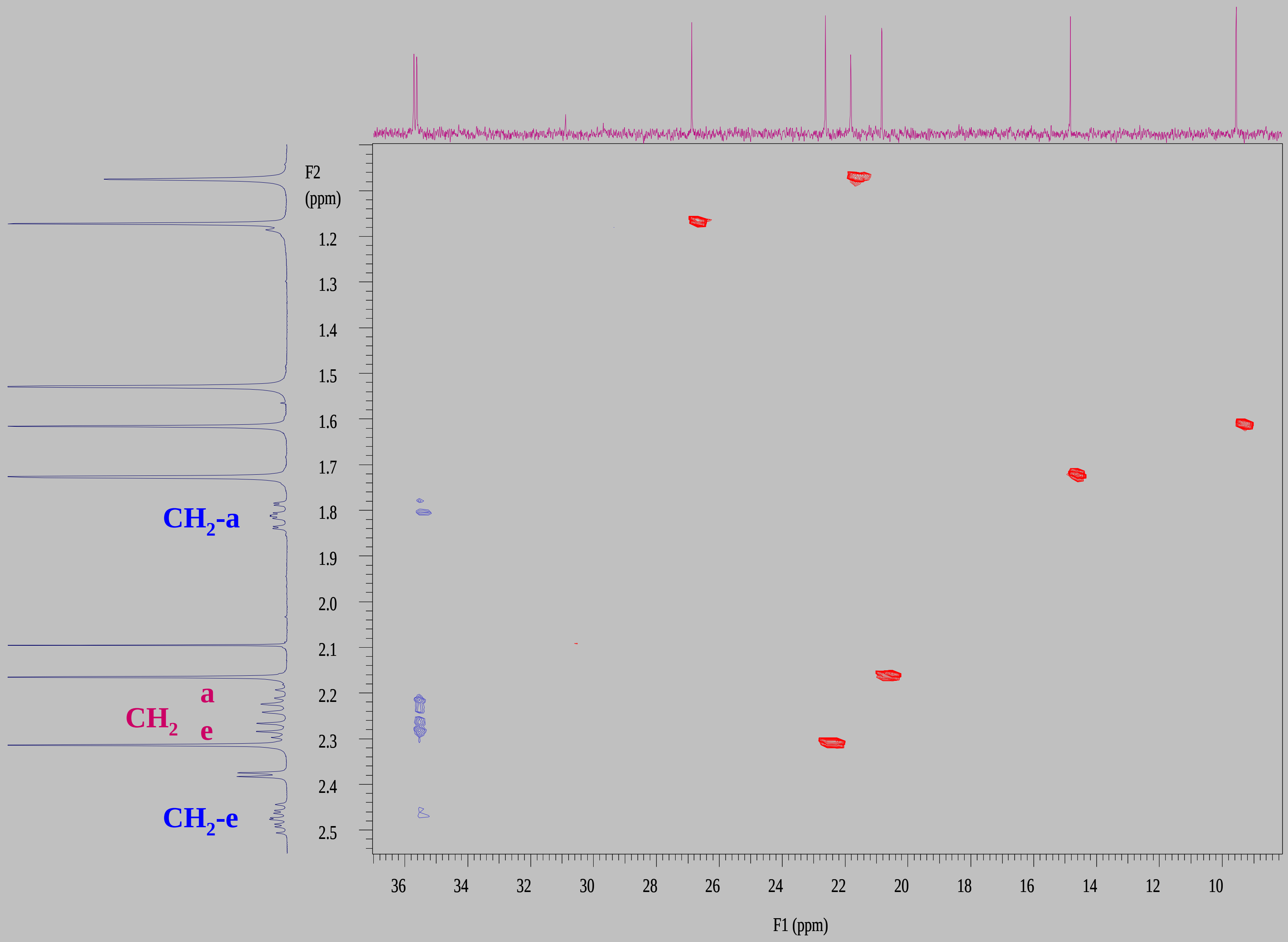




Gradient HSQC spectrum of Taxol (expansion #2)

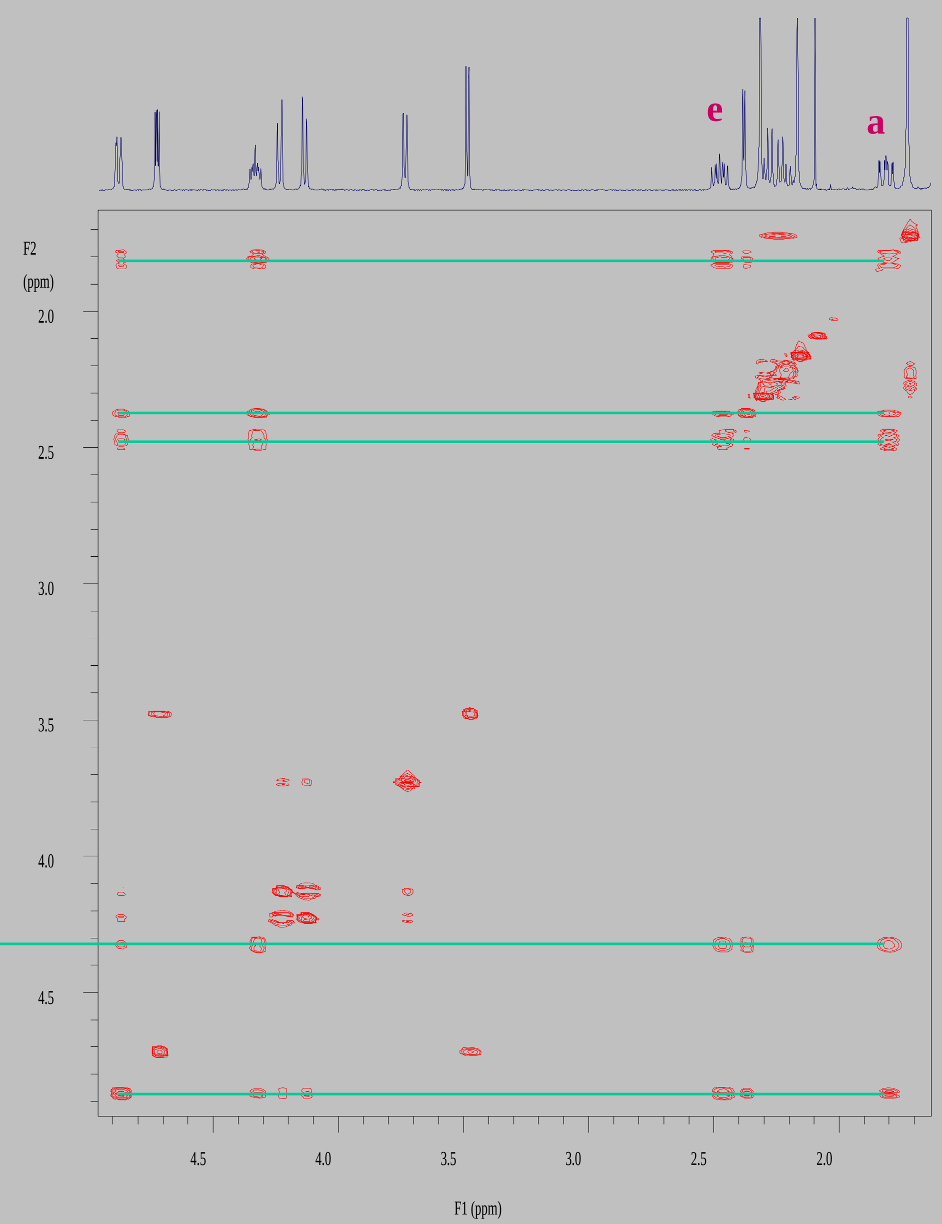


Gradient HSQC spectrum of Taxol (expansion #3)



[1]H TOCSY spectrum of Taxol

(expansion #4)



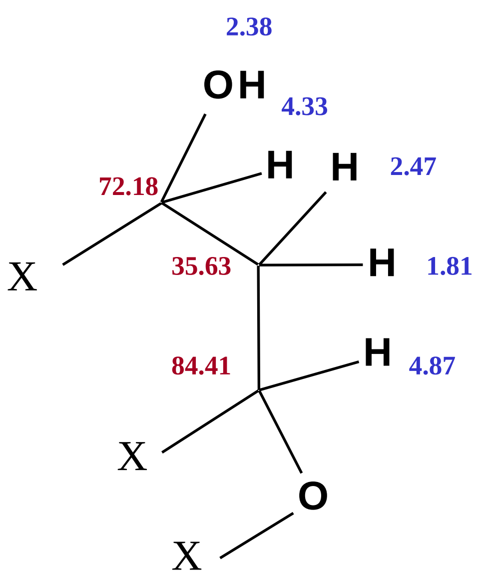
4.87, 4.33, 2.47, 2.38, 1.81

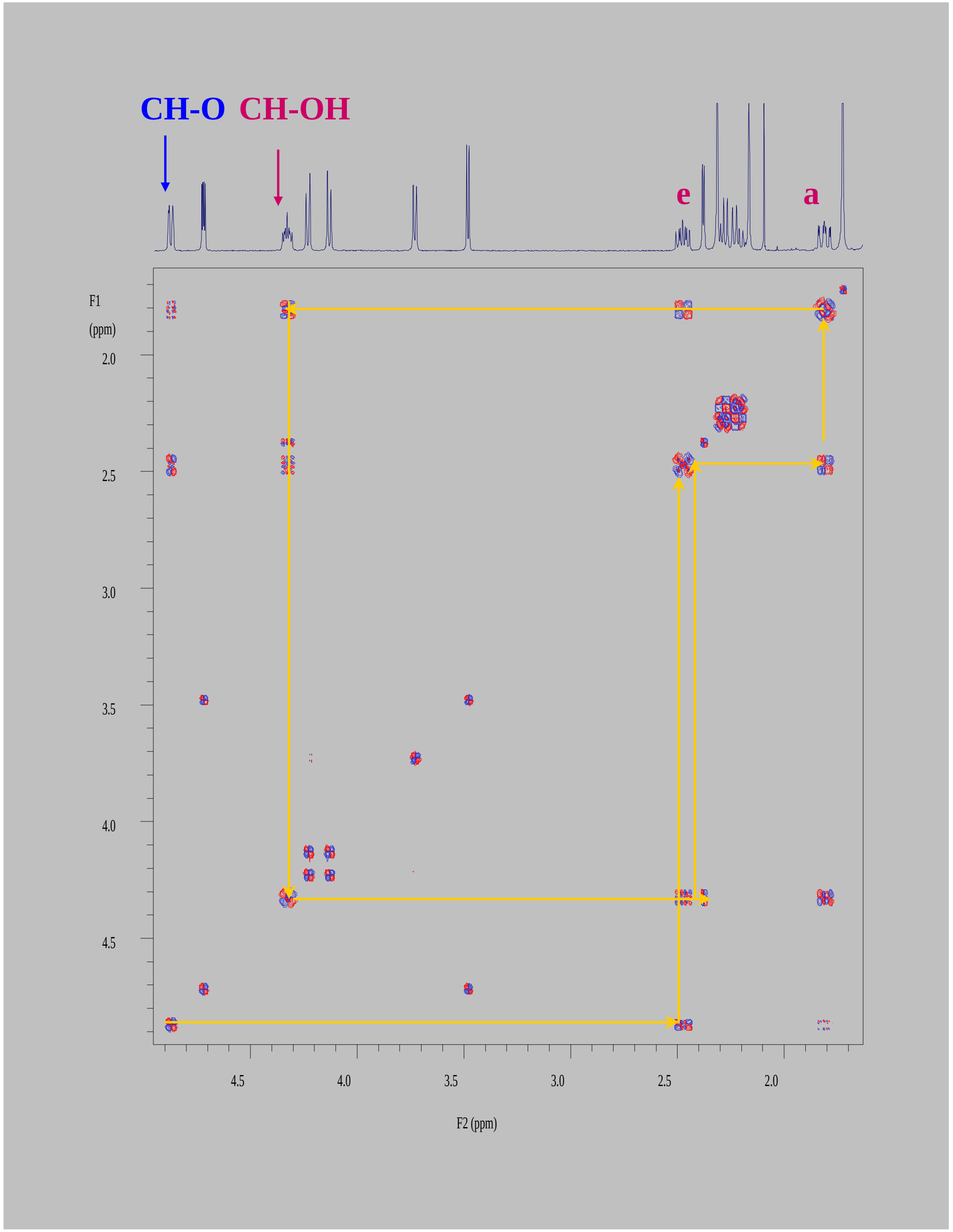
DQF-COSY of Taxol

(expansion #4)

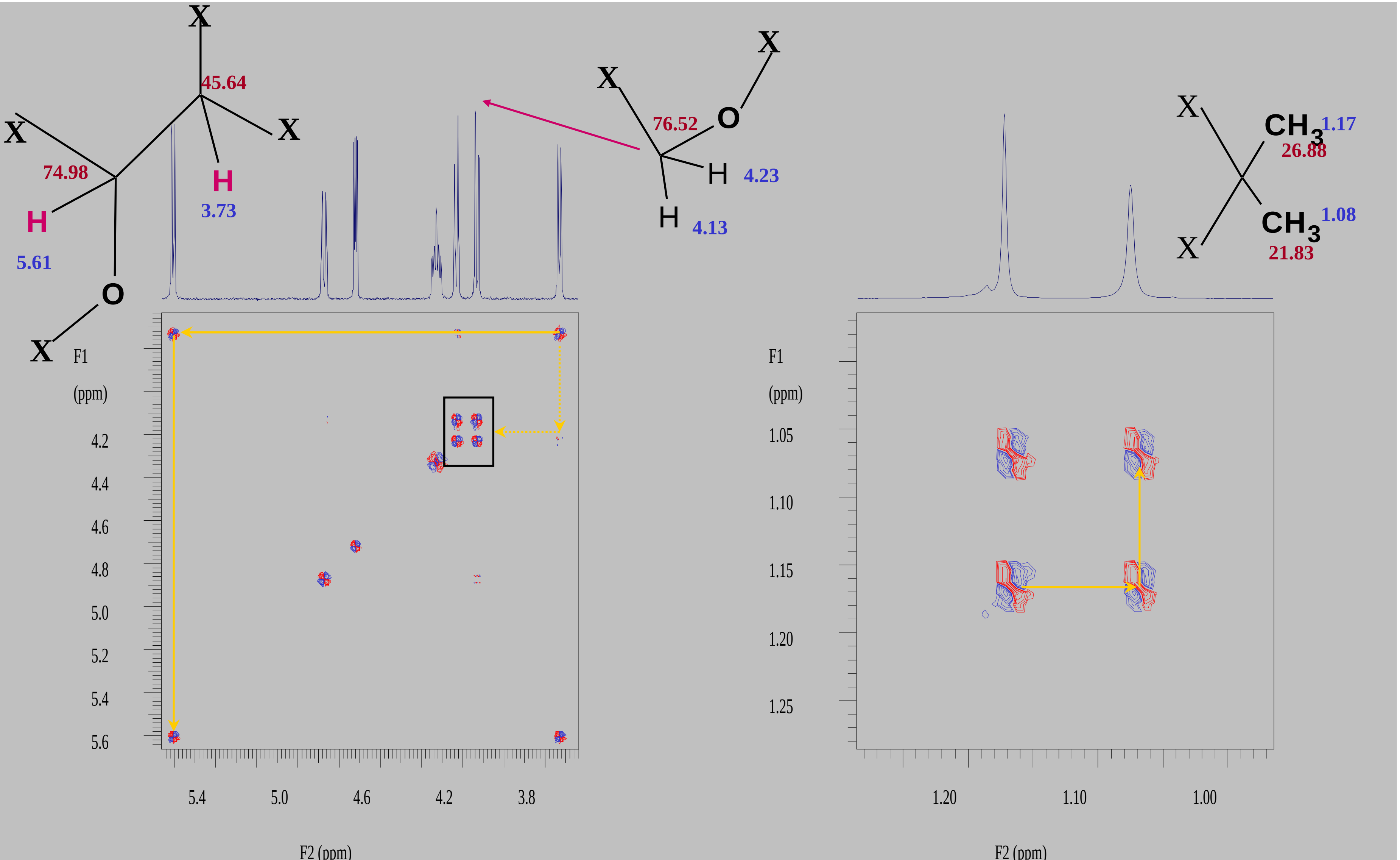
Known from TOCSY:
4.87, 4.33, 2.47, 2.38, 1.81

Known from HSQC:
2.47, 1.81 are geminal partners
2.38 is OH





DQF-COSY of Taxol (expansion #5)



Known from HSQC: 4.23 and 4.13 are geminal partners

Assigned substructures:

8.06 (2)	130.21 (d*)	6.16 (1)	72.41 (d)
7.44 (2)	128.70 (d*)	2.29 (1); 2.22 (1)	35.72 (t)
7.54 (1)	133.71 (d)	1.72 (3)	14.83 (q)
7.67 (2)	127.04 (d*)	5.61 (1)	74.98 (d)
7.33 (2)	128.72 (d*)	3.73 (1)	45.64 (d)
7.42 (1)	131.97 (d)		
		4.87 (1)	84.41 (d)
7.41 (2)	127.04 (d*)	4.33 (1)	72.18 (d)
7.35 (2)	129.03 (d*)	2.47 (1); 1.81 (1)	35.63 (t)
7.28 (1)	128.37 (d)	2.38 (1)	
6.91 (1)		4.23 (1); 4.13 (1)	76.52 (t)
5.72 (1)	55.04 (d)		
4.72 (1)	73.20 (d)	1.17 (3)	26.88 (q)
3.48 (1)		1.08 (3)	21.83 (q)

To be assigned:

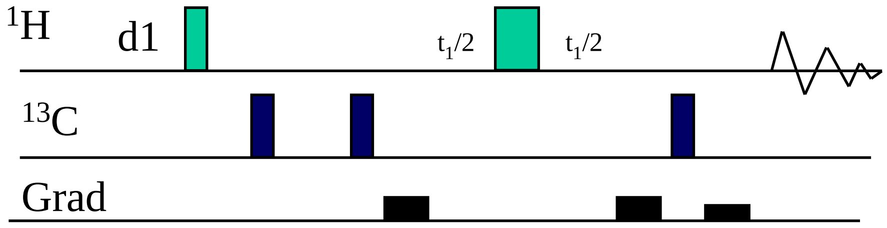
6.21 (1)	75.57 (d)
2.31 (3)	22.63 (q)
2.17 (3)	20.84 (q)
1.73 (1)	
1.62 (3)	9.57 (q)

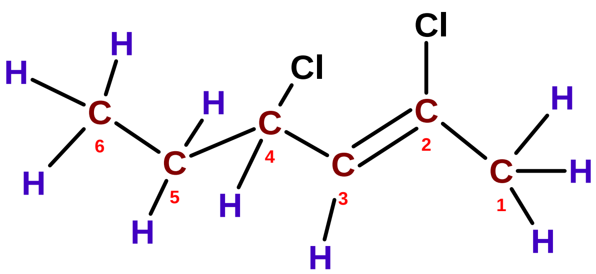
203.61, 172.72, 171.22, 170.35, 167.04,
167.01, 141.95, 137.99, 133.65, 133.23,
129.18, 81.19, 79.05, 58.65, 43.19

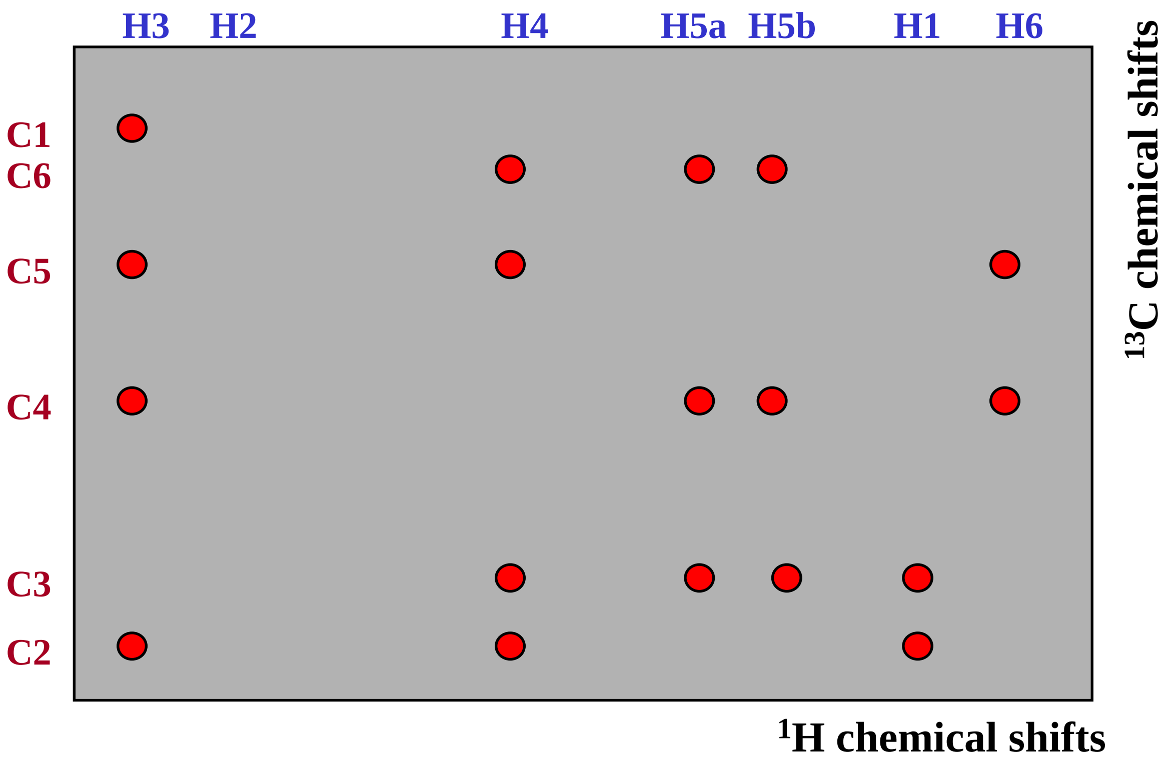
Number of assigned substructures: 9

HMBC - Heteronuclear Multiple Bond Coherence

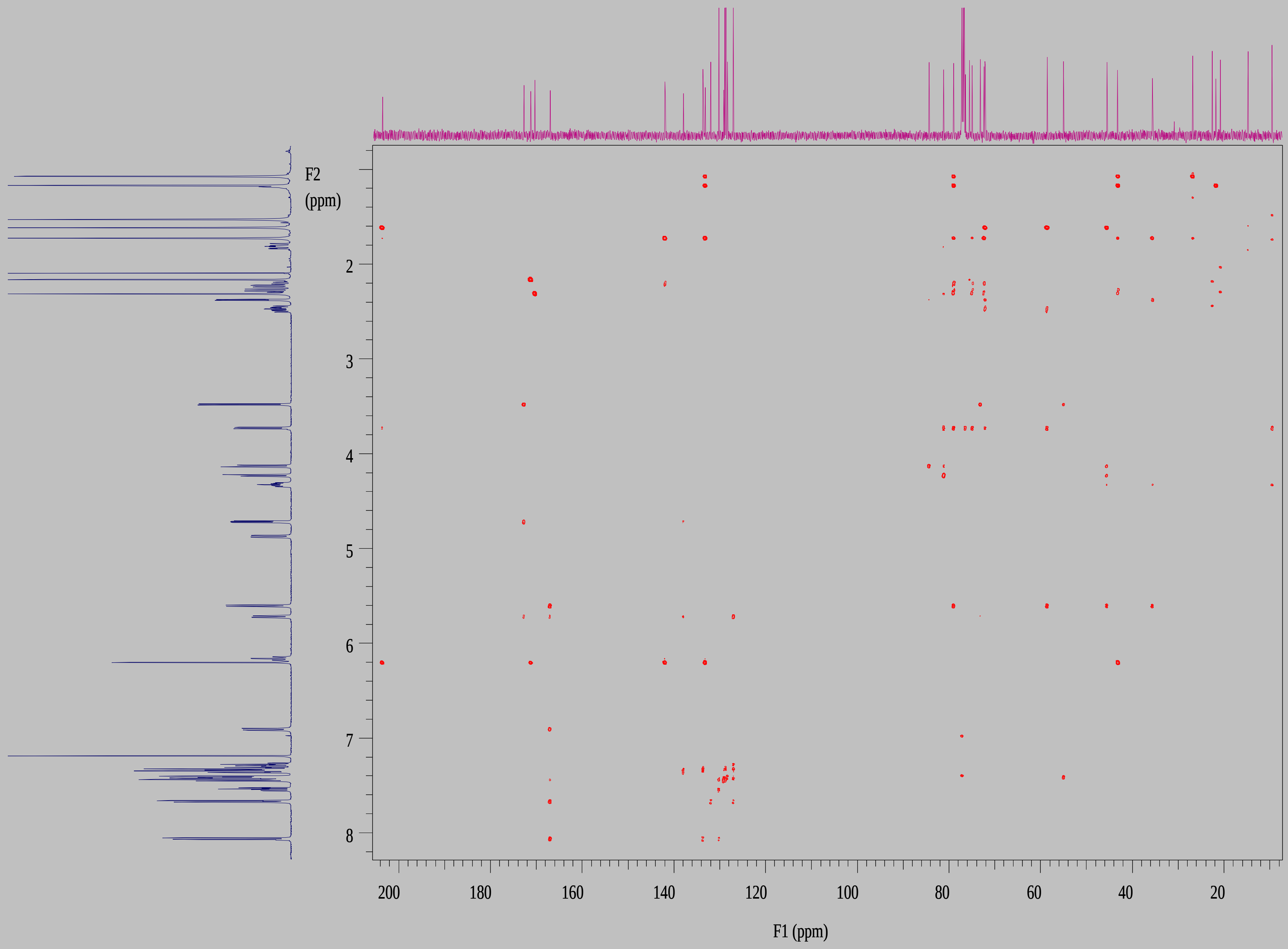
(correlates ^{13}C-^{1}H chemical shifts via long-range $^{n}J(X,H)$ (n=2,3,4?) couplings)



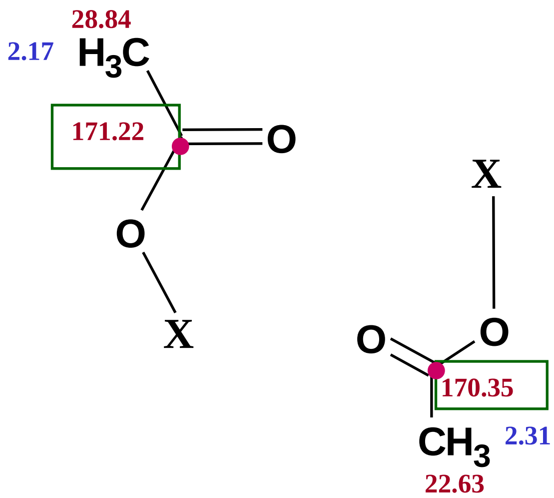


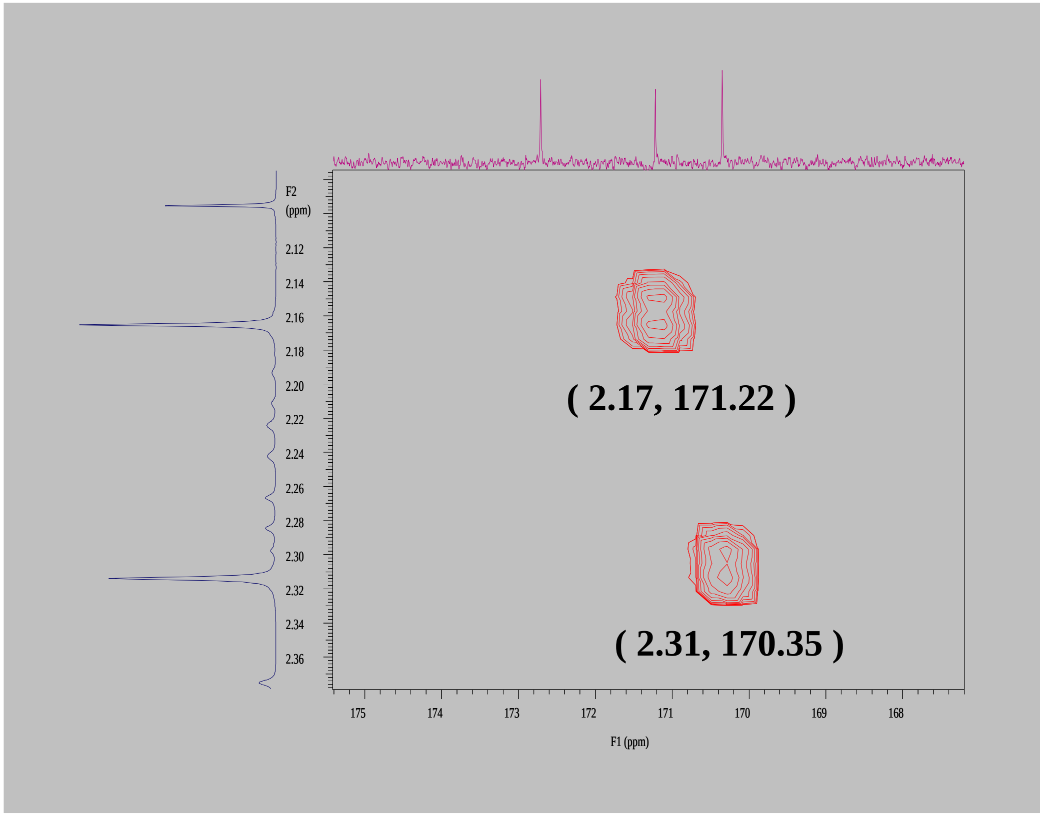


Gradient HMBC Spectrum of Taxol



Gradient HMBC spectrum of Taxol (expansion #1)





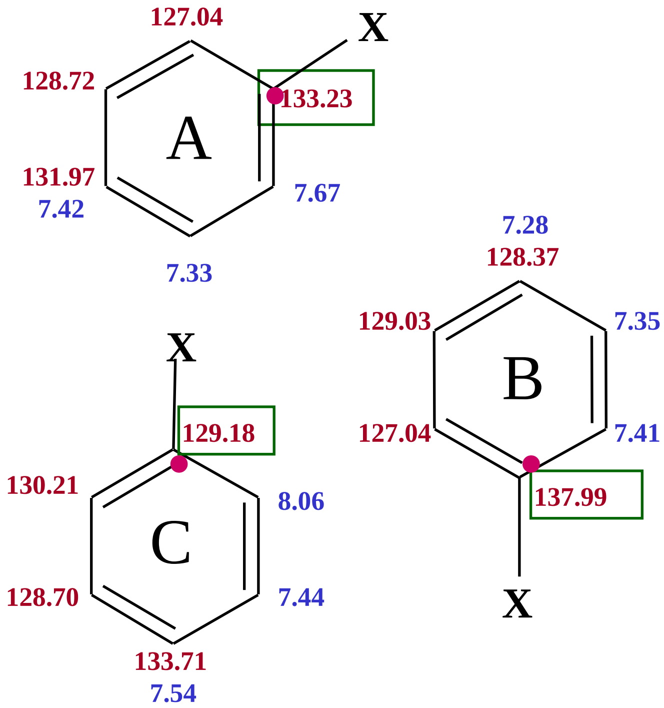
To be assigned:

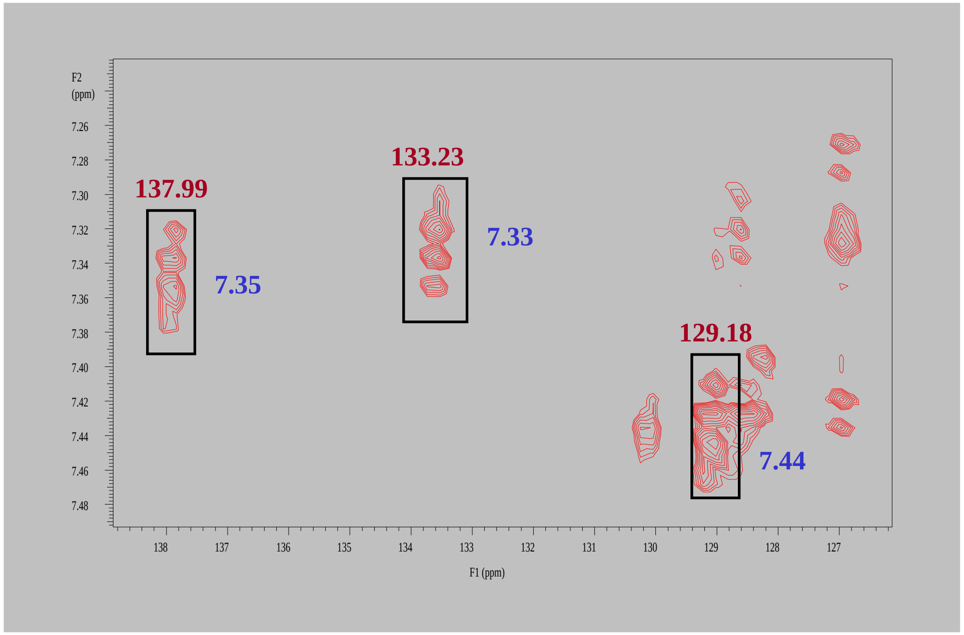
6.21	(1)	75.57	(d)
2.31	(3)	22.63	(q)
2.17	(3)	20.84	(q)
1.73	(1)		
1.62	(3)	9.57	(q)

203.61, 172.72, 171.22, 170.35, 167.04, 167.01, 141.95, 137.99, 133.65, 133.23, 129.18, 81.19, 79.05, 58.65, 43.19

Number of assigned substructures: 11

Gradient HMBC spectrum of Taxol (expansion #2)





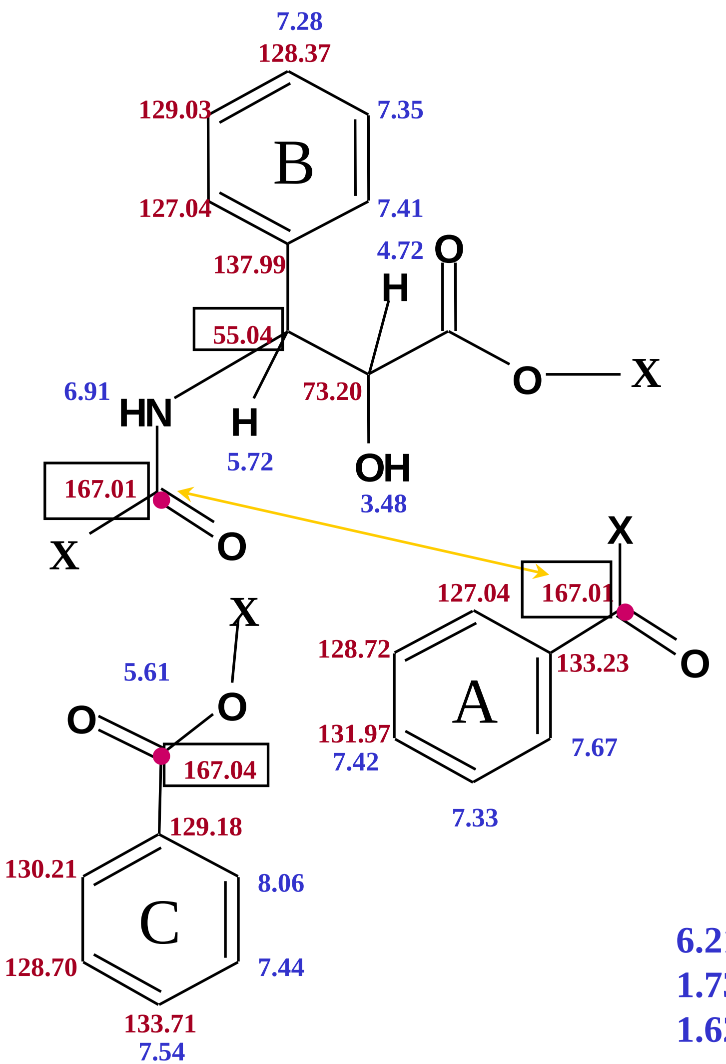
To be assigned:

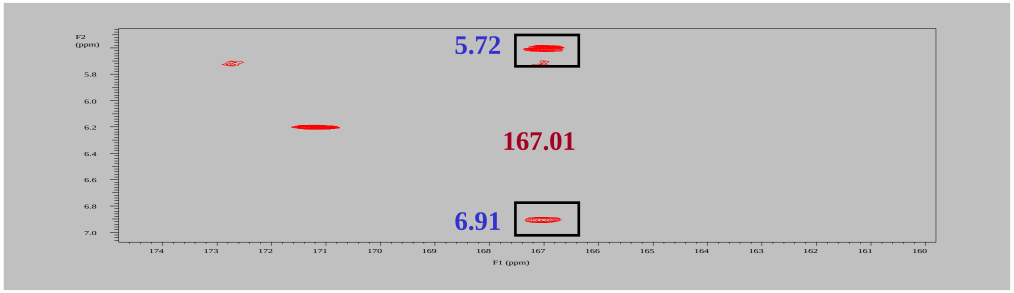
6.21 (1) 75.57 (d)
1.73 (1)
1.62 (3) 9.57 (q)

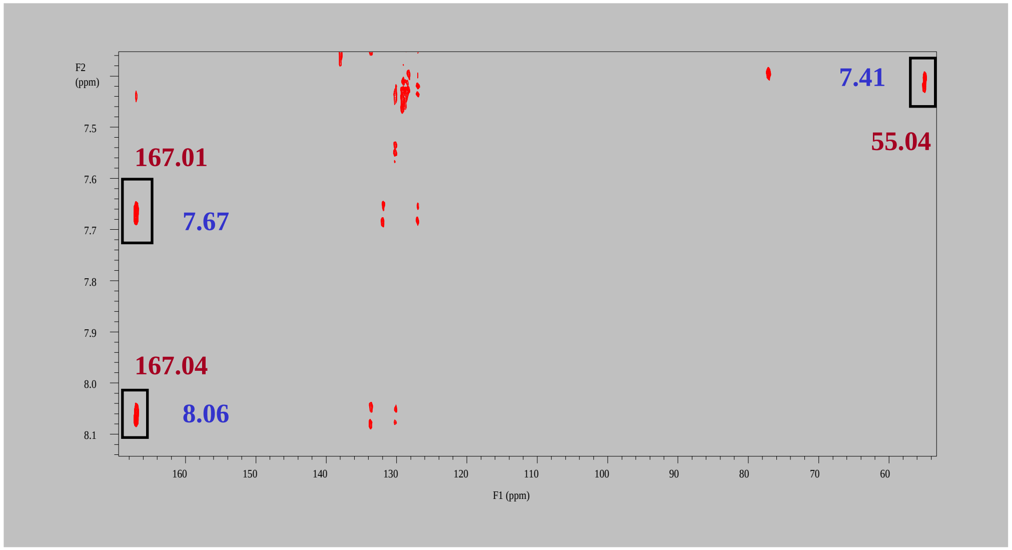
203.61, 172.72, 167.04, 167.01, 141.95, 137.99,
133.65, 133.23, 129.18, 81.19, 79.05, 58.65, 43.19

Number of substructures to link: 11

Gradient HMBC spectrum of Taxol (expansion #3)







To be assigned:

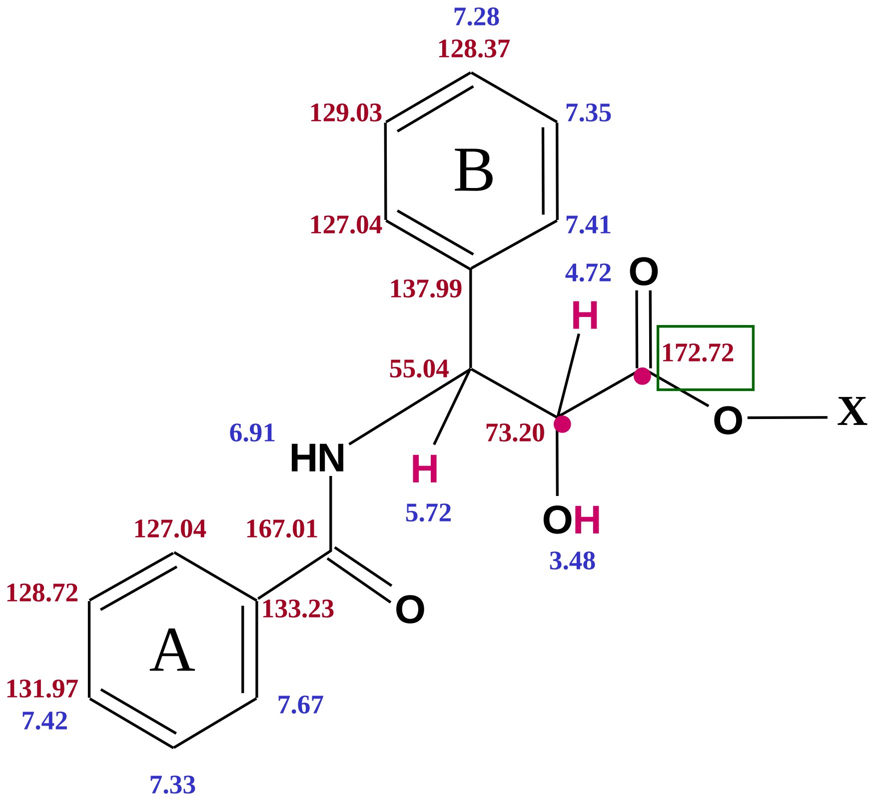
6.21 (1) 75.57 (d) 203.61, 172.72, 167.04, 167.01, 141.95,

1.73 (1) 133.65, 81.19, 79.05, 58.65, 43.19

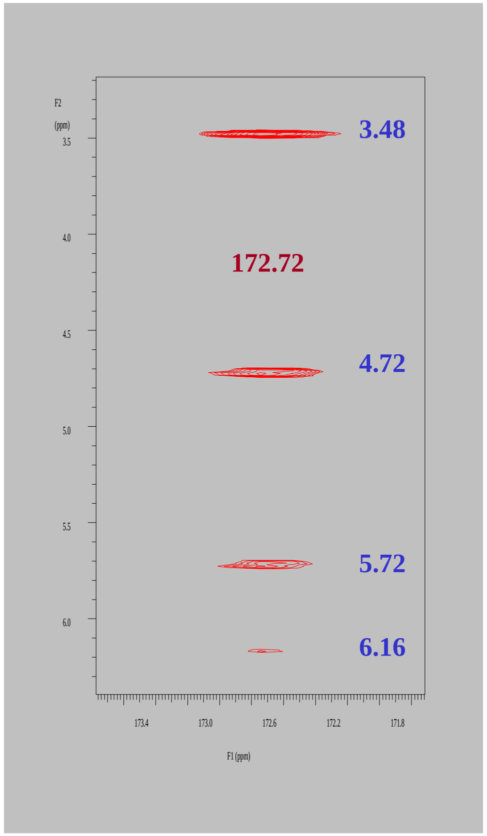
1.62 (3) 9.57 (q)

Number of substructures to link: 9

Gradient HMBC spectrum of Taxol (expansion #4)



(6.16)!!

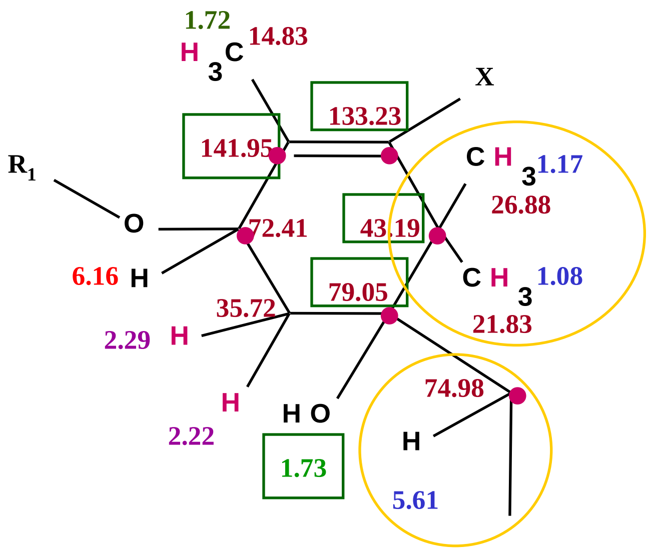


To be assigned:

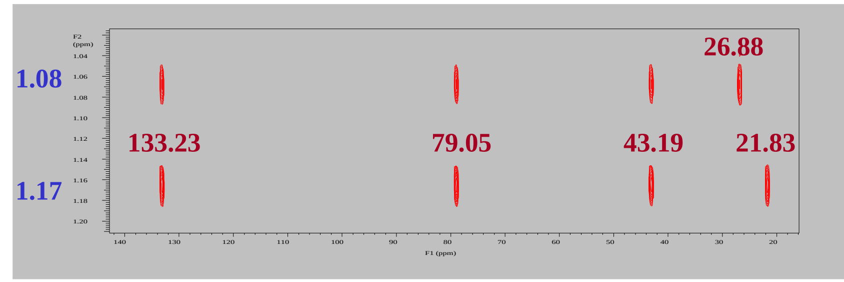
6.21 (1)	75.57 (d)	203.61, 172.72, 141.95, 133.65,
1.73 (1)		81.19, 79.05, 58.65, 43.19
1.62 (3)	9.57 (q)	

Number of substructures to link: 9

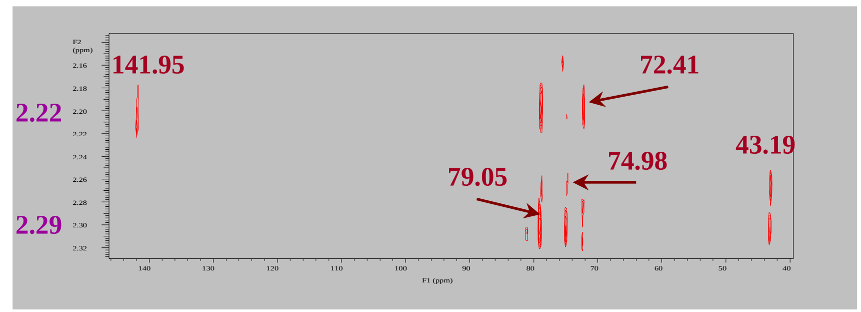
Gradient HMBC spectrum of Taxol (expansion #5)



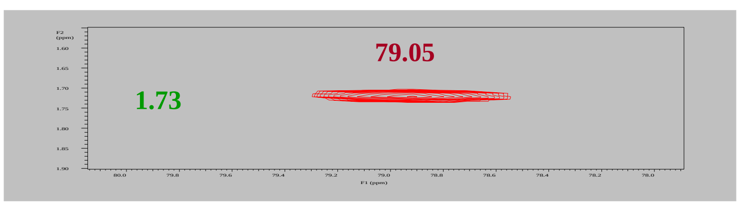
c



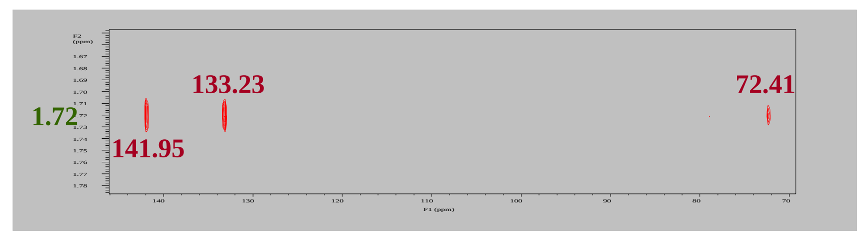
b



d



a

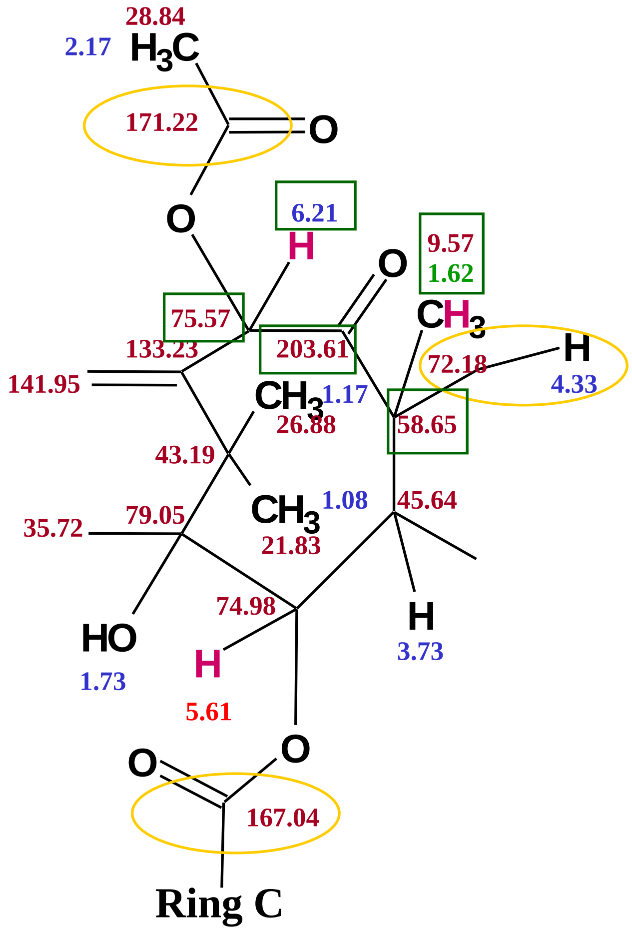


To be assigned:

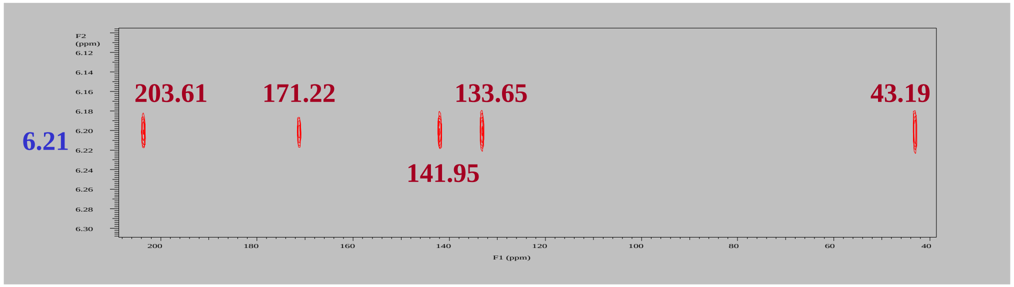
6.21 (1)	75.57 (d)	203.61, 141.95, 133.65,
1.73 (1)		81.19, 79.05, 58.65, 43.19
1.62 (3)	9.57 (q)	

Number of substructures to link: 6

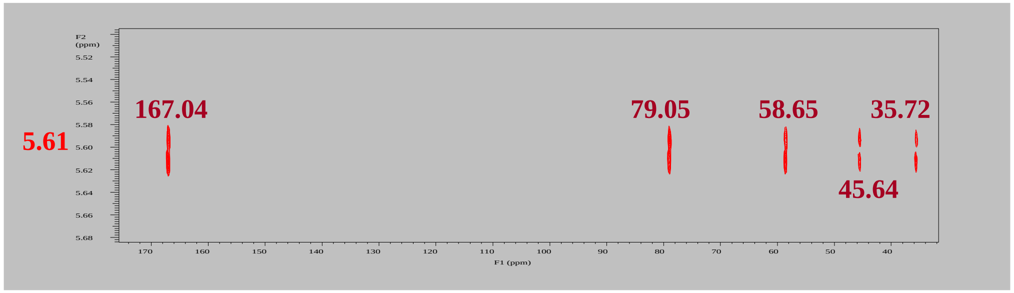
Gradient HMBC spectrum of Taxol (expansion #6)



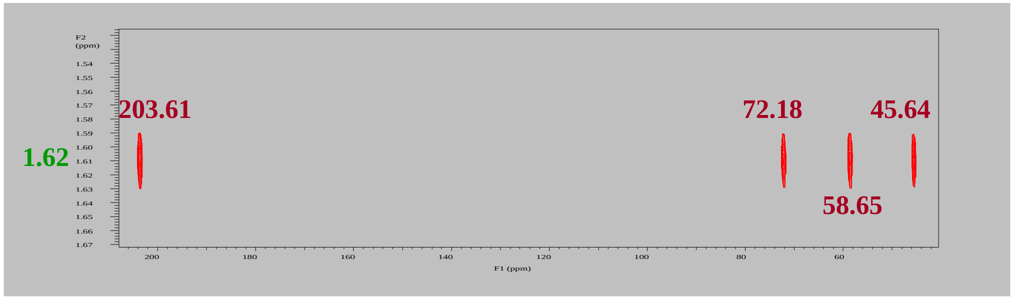
a



b



c

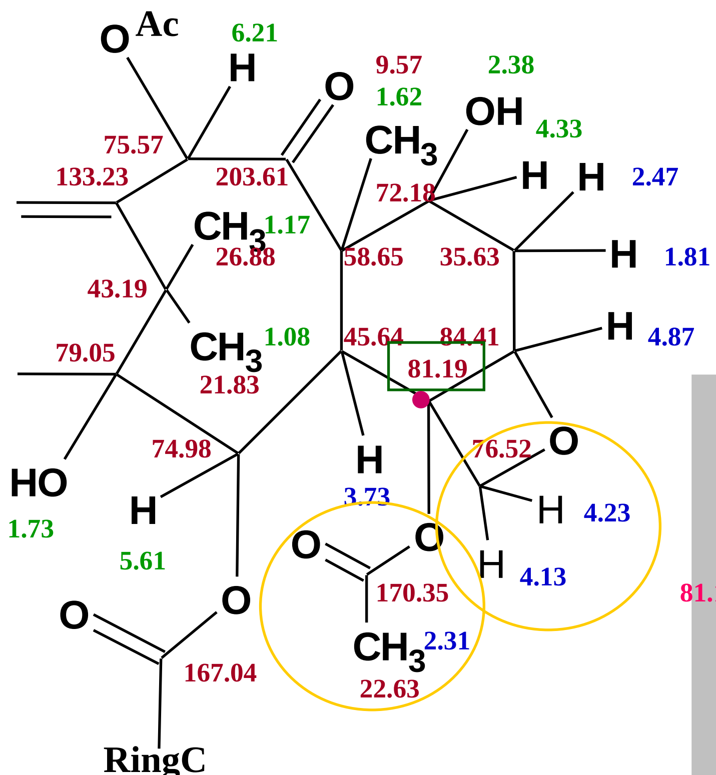


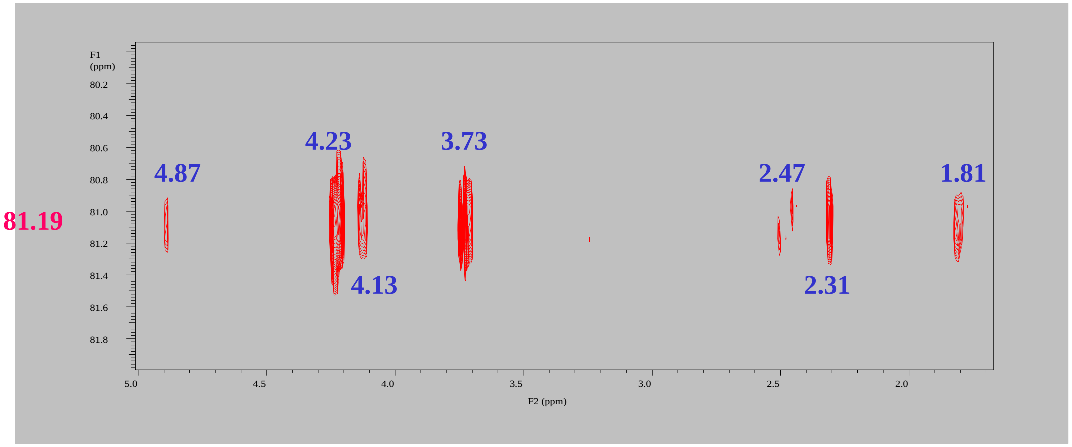
To be assigned:

6.21 (1)	75.57 (d)	203.61, 81.19, 58.65
1.62 (3)	9.57 (q)	

Number of substructures to link: 3

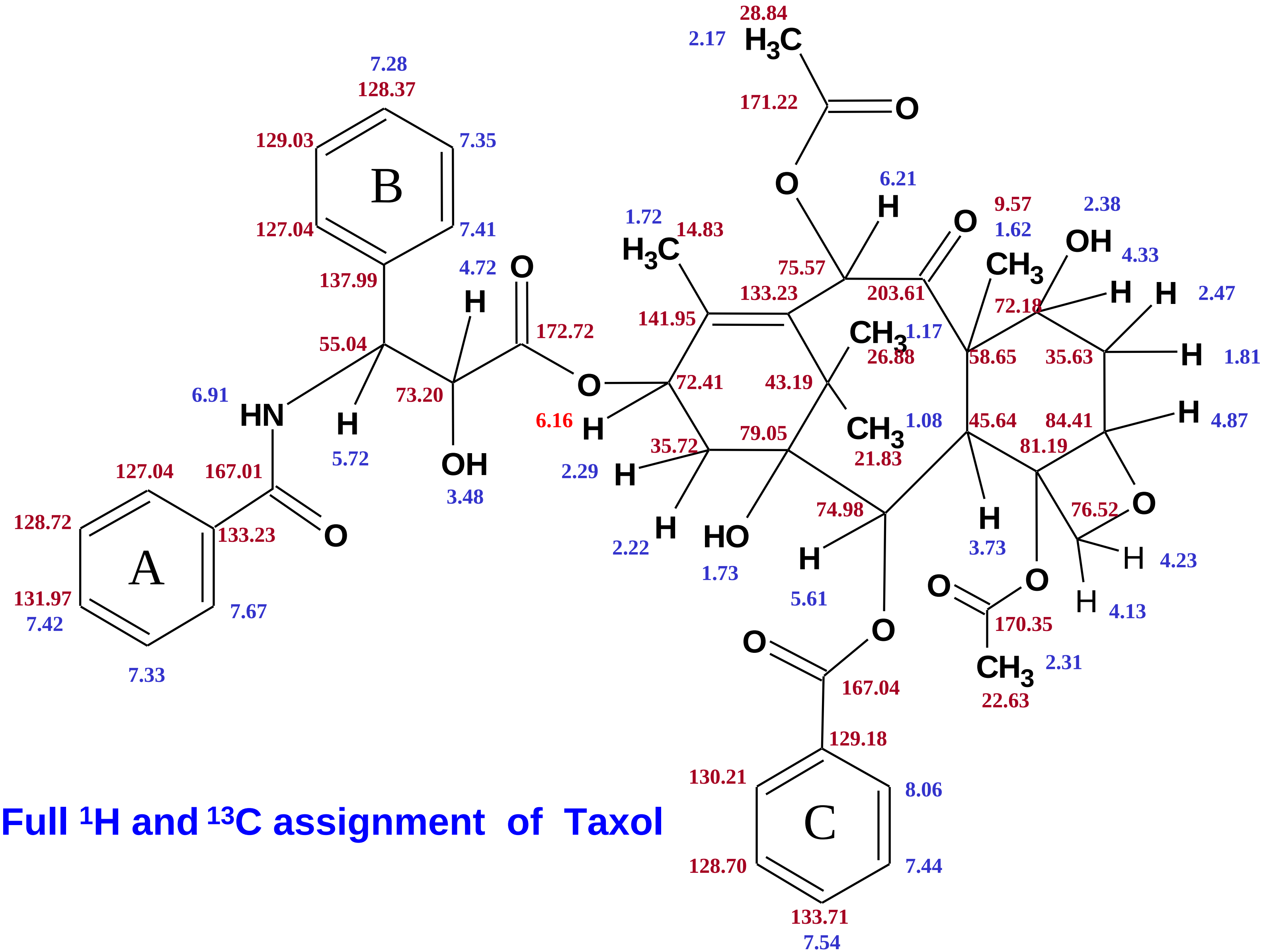
Gradient HMBC spectrum of Taxol (expansion #7)





To be assigned: 81.19

Number of substructures to link: 0 !!!!

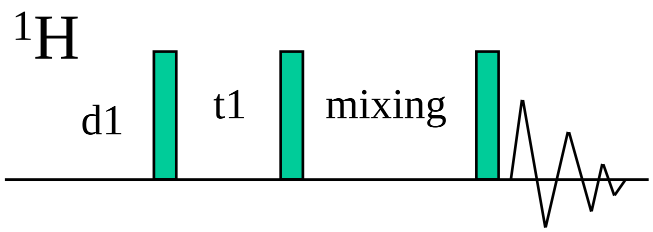


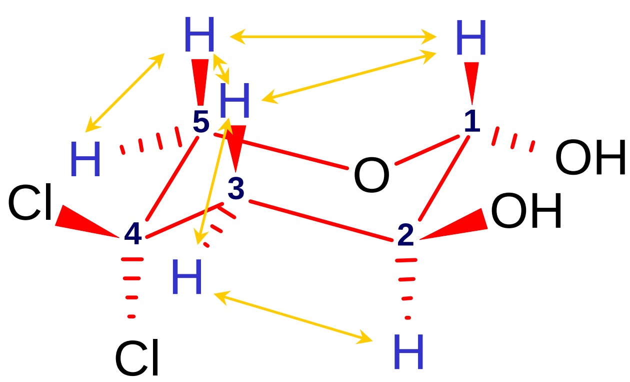
Full ^{1}H and ^{13}C assignment of Taxol

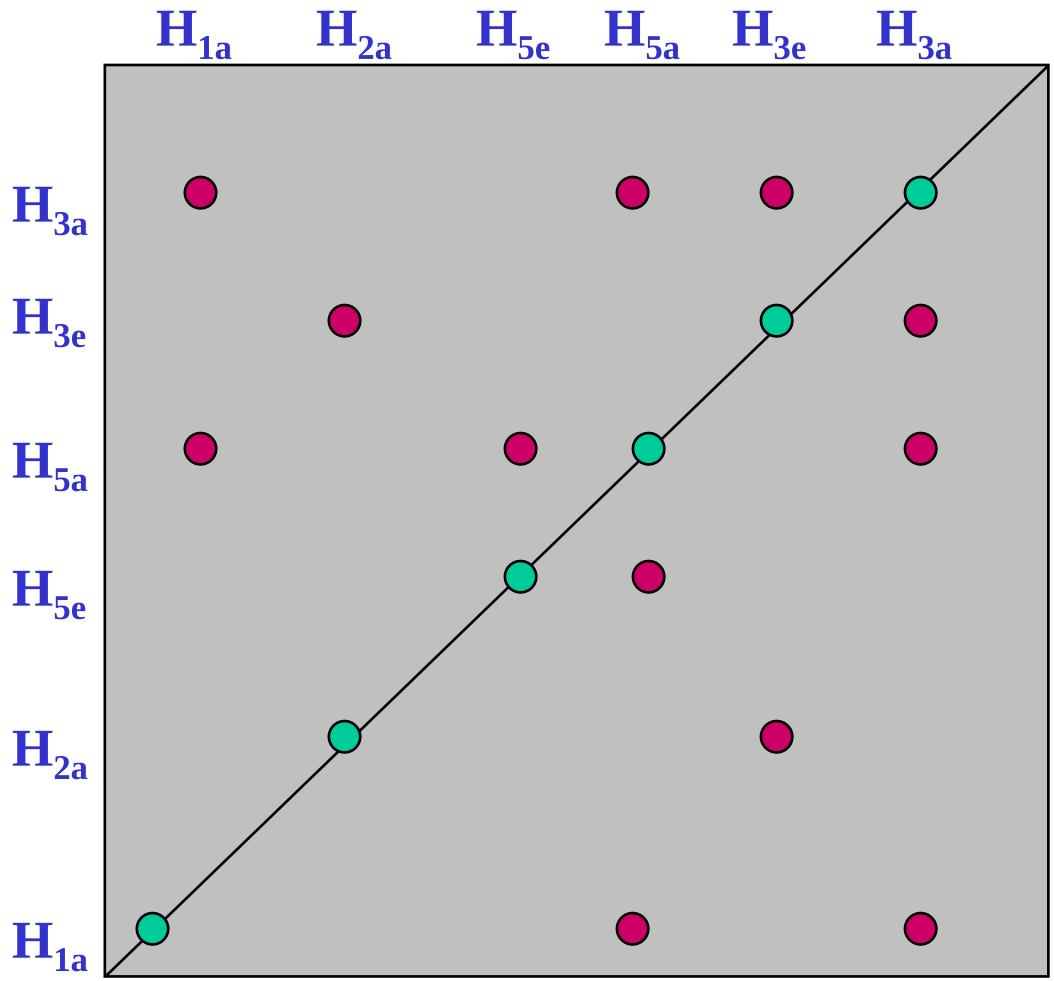
NOESY - Nuclear Overhauser Enhanced SpectroscopY

(detects protons close in space or in chemical exchange)

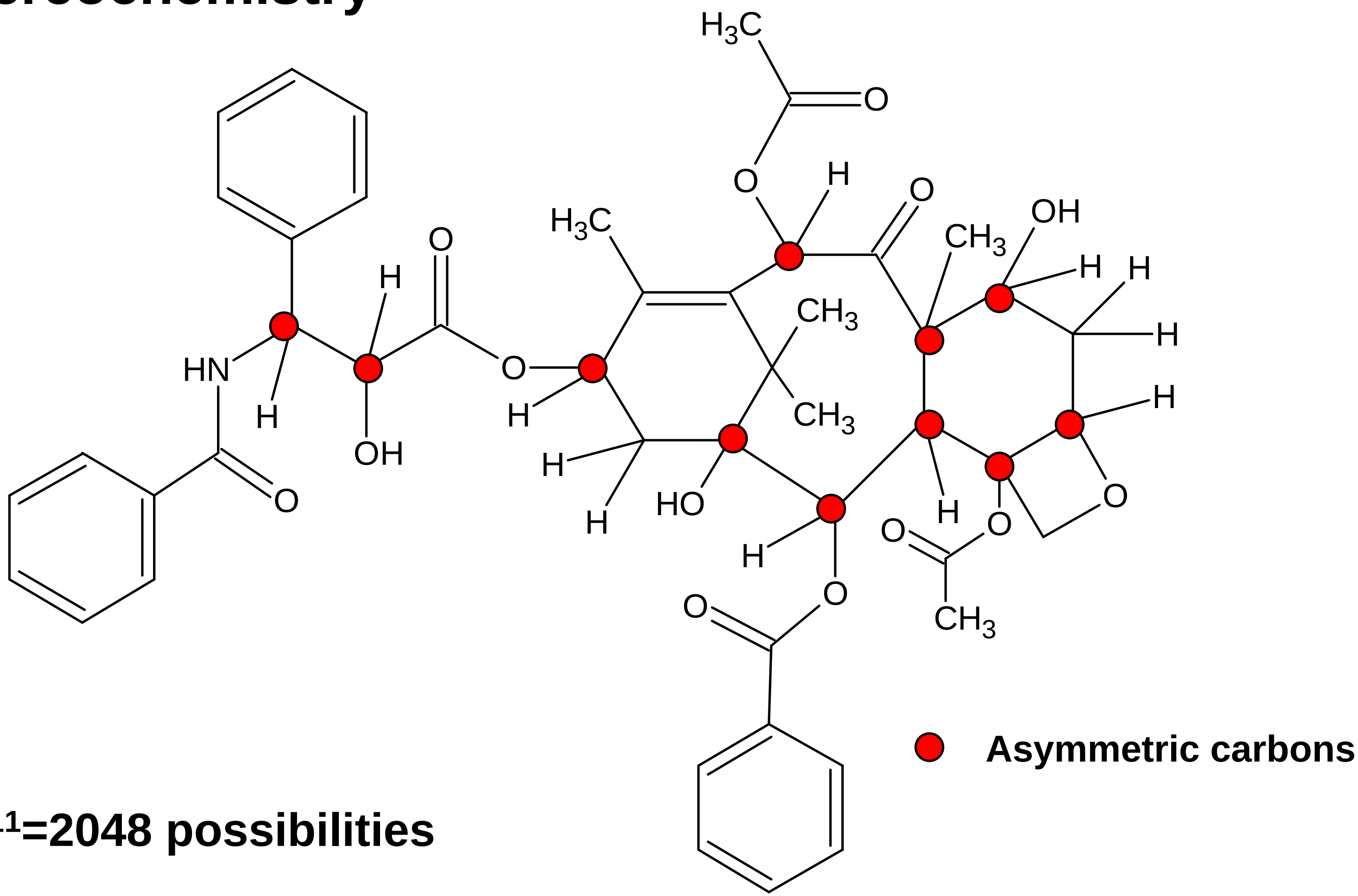
$$\mathbf{noe = f(1/r^6)}$$







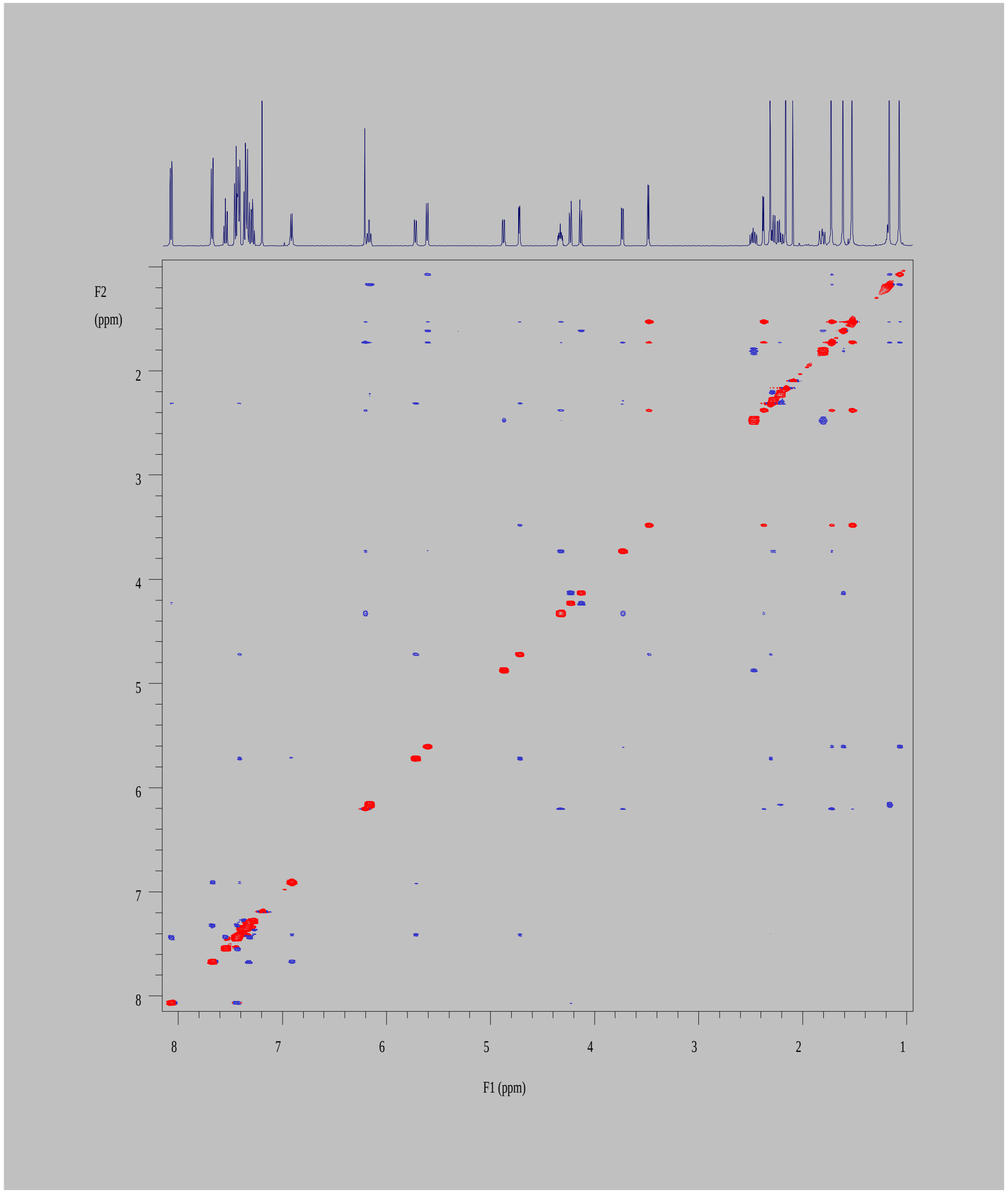
Stereochemistry



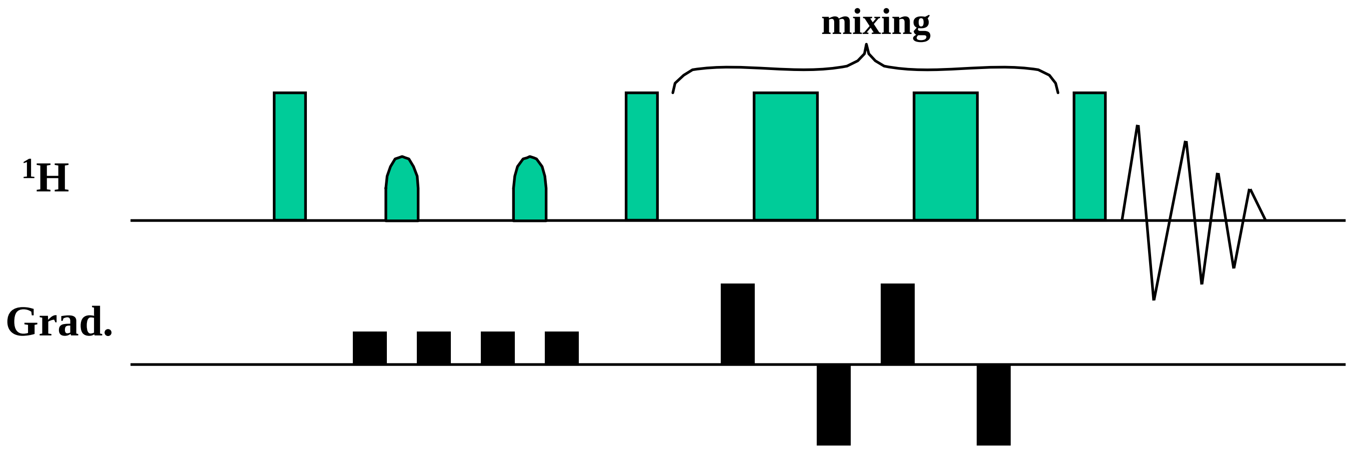
2^{11}=2048 possibilities

^{1}H NOESY of Taxol

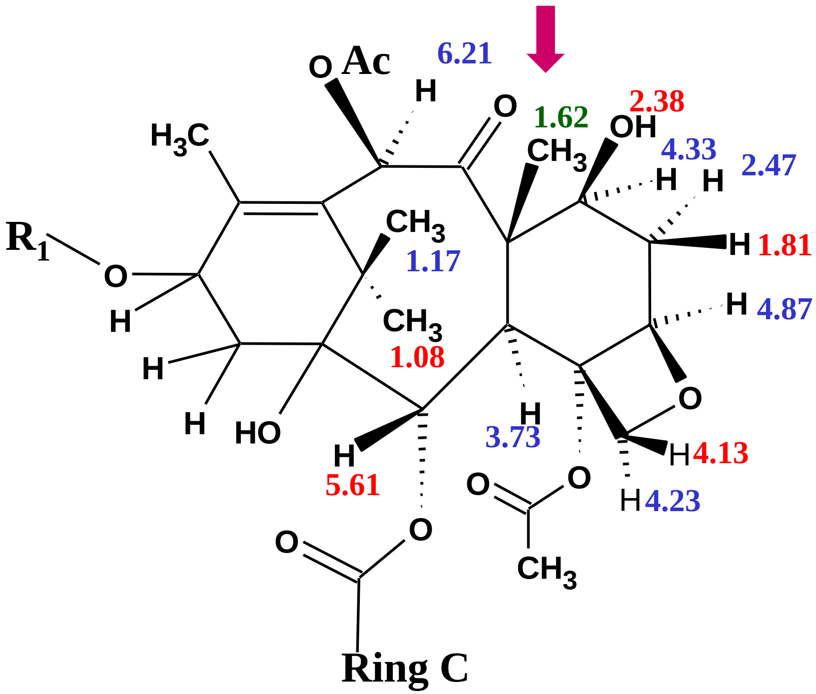
nt=4 per increment
256 complex pints in F1
mix=700 msec
exp. time=2 h 10 min



DPFGSE - NOE (Double Pulsed Field Gradient Spin Echo NOE)



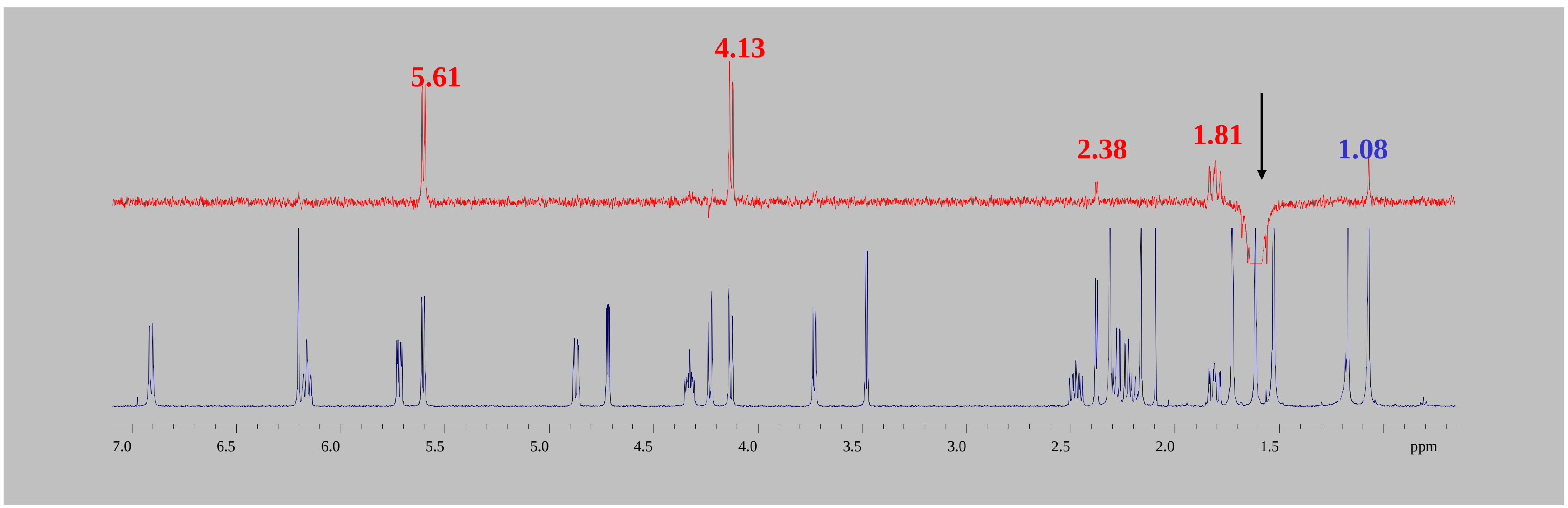
1D Gradient version of NOESY with extreme reliable results
Replaces the 1D NOE-difference experiment



DPFGNOE spectrum of Taxol

Selective inversion at 1.62 ppm

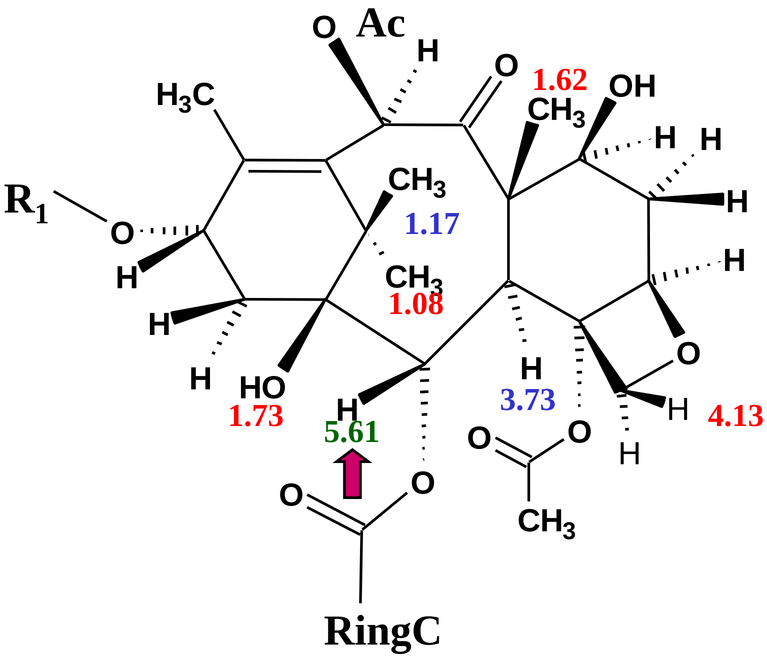
Experiment time: 4 min

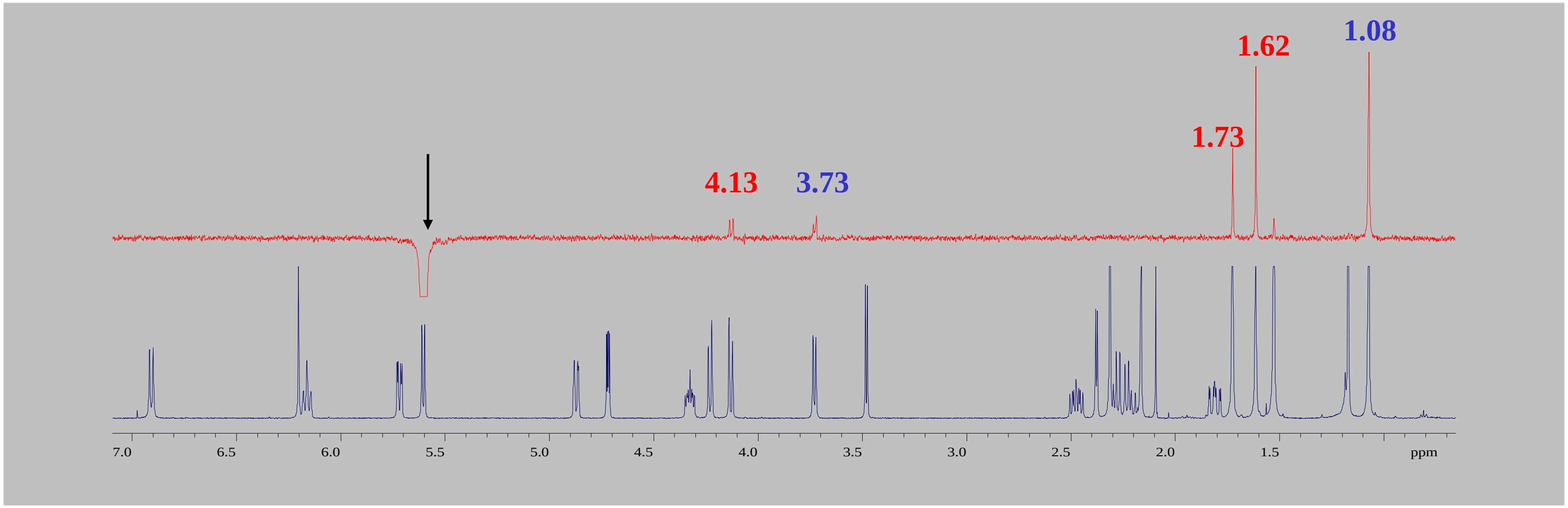


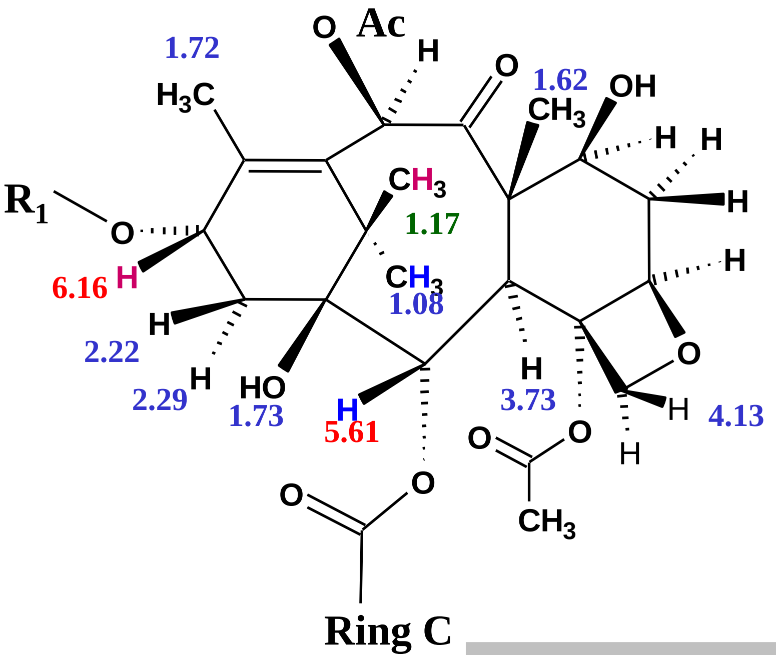
DPFGNOE spectrum of Taxol

Selective inversion at 5.61 ppm

Experiment time: 4 min

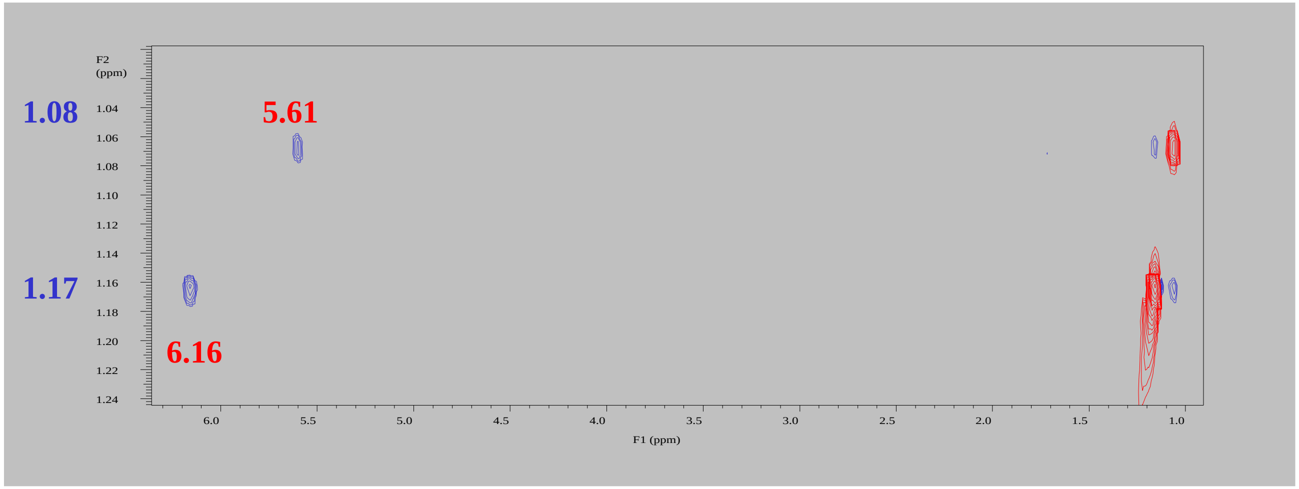






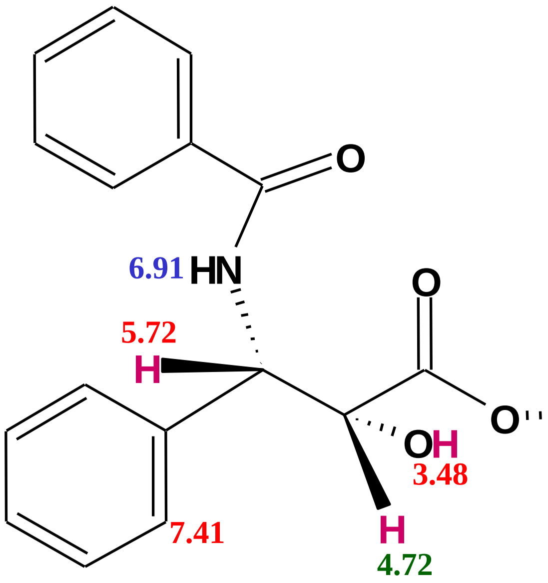
^{1}H NOESY spectrum of Taxol

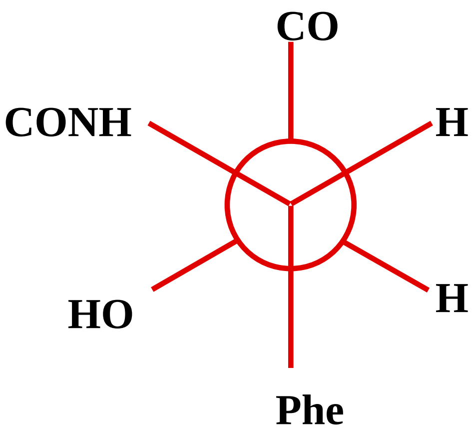
(expansion)



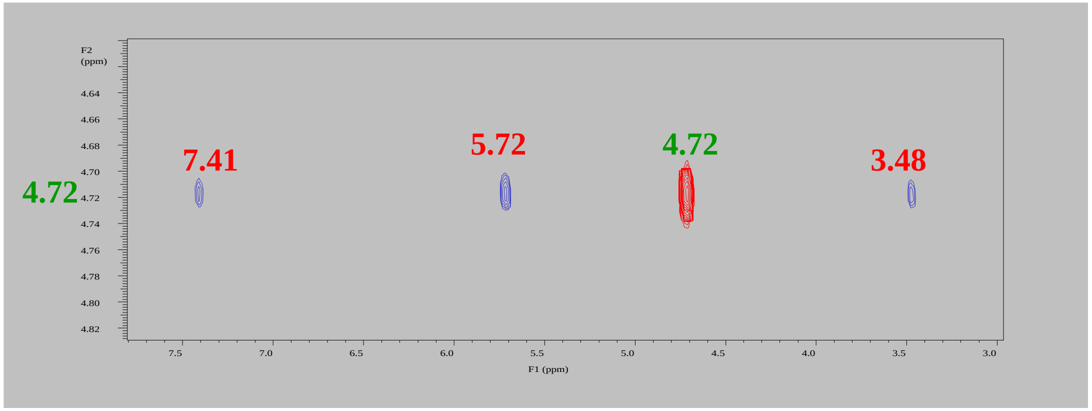
^{1}H NOESY spectrum of Taxol

(expansion)

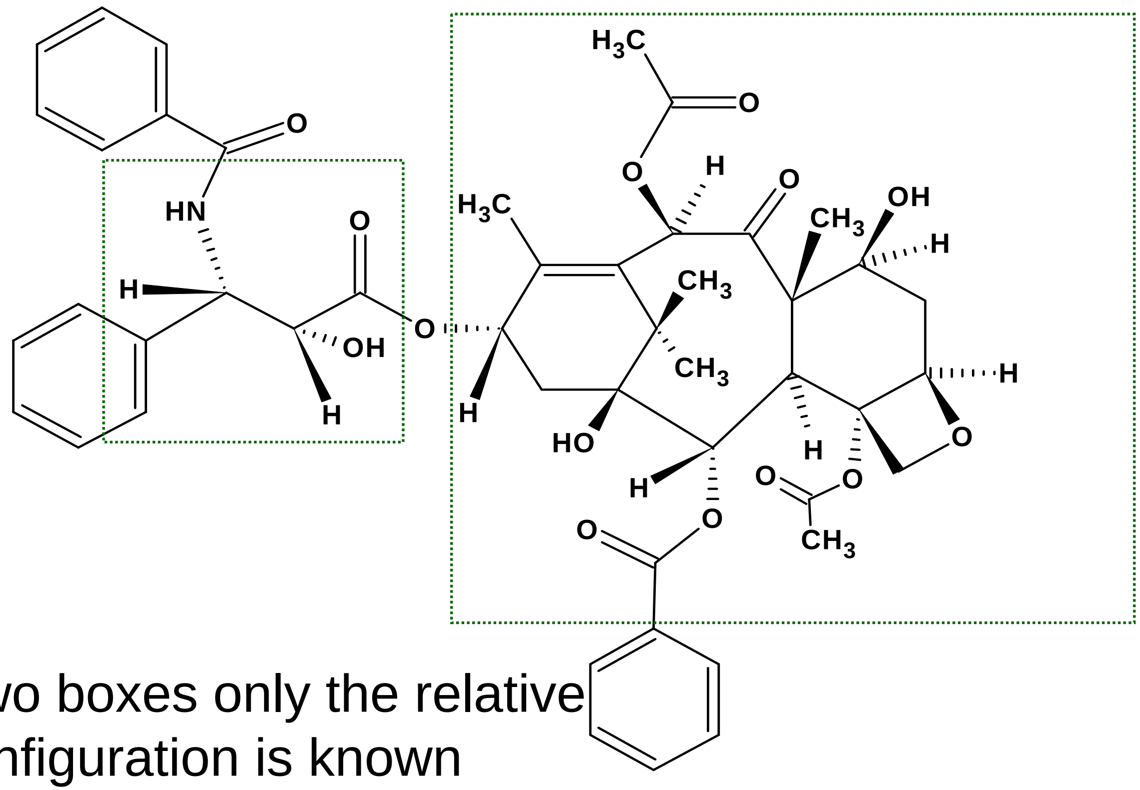




$^3J(HH) = 2.7$ Hz



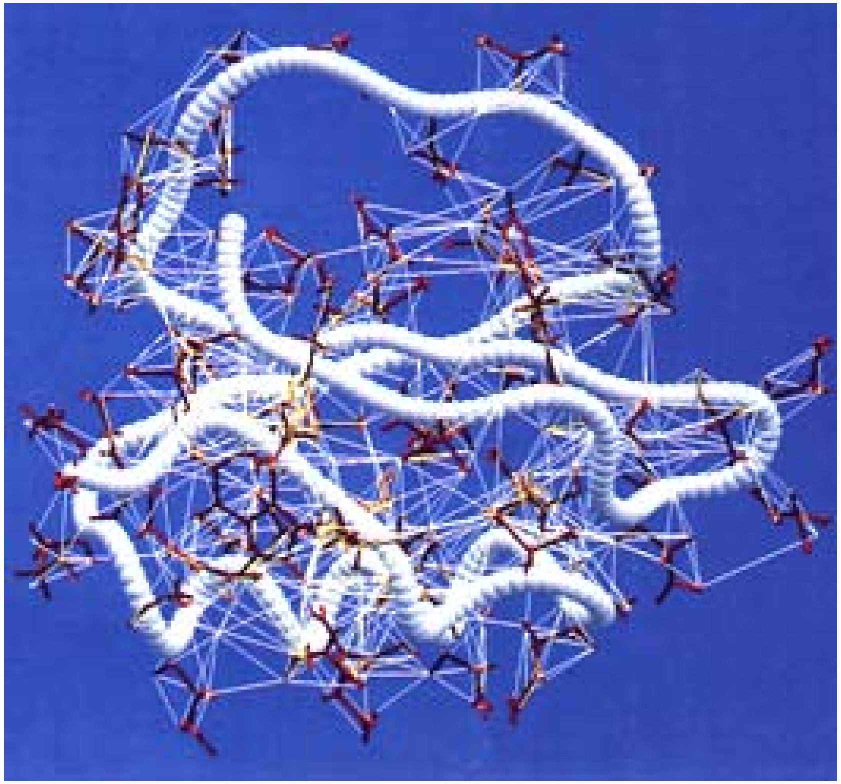
Stereo Structure of Taxol



In the two boxes only the relative configuration is known

Applications of NMR

3D Structure of Bio-macromolecules



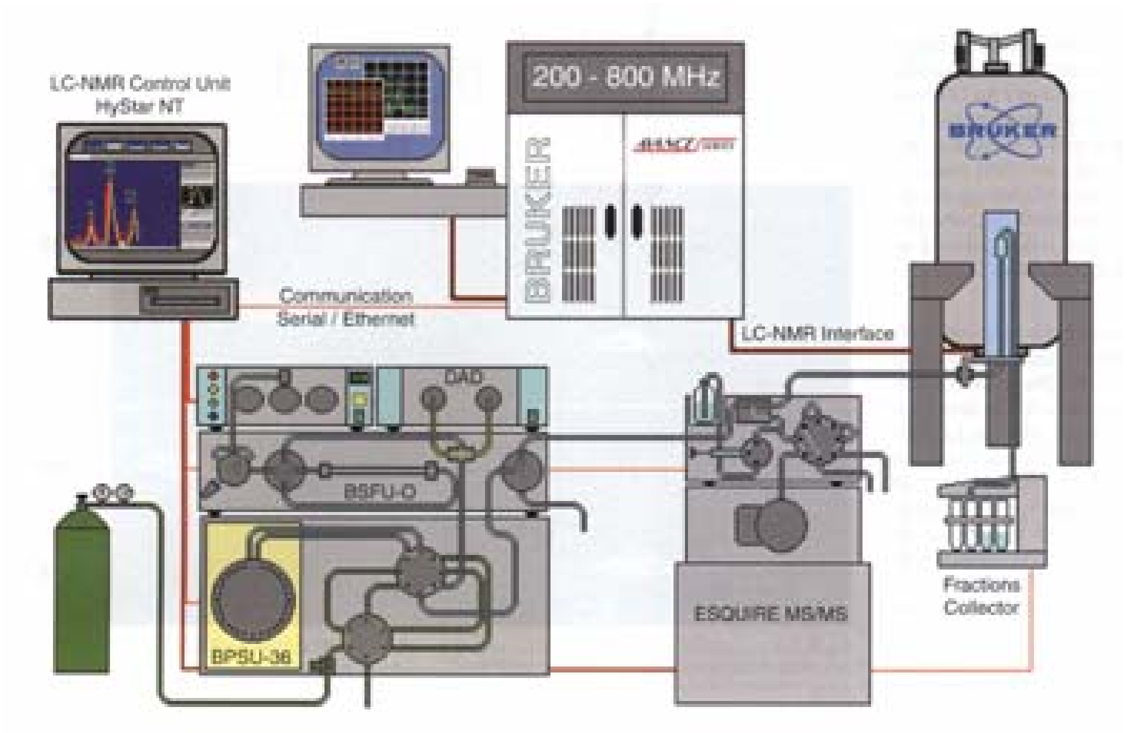


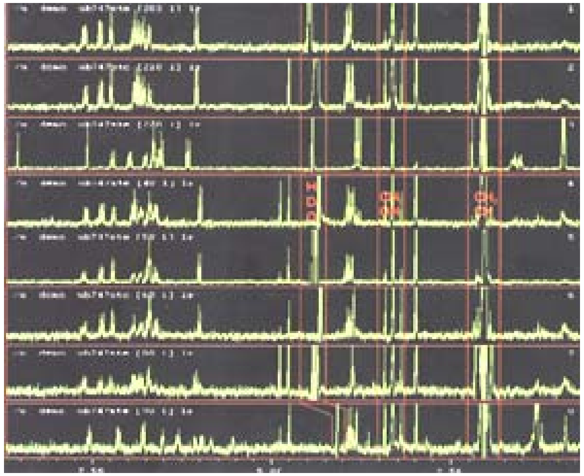
K. Wuethrich

2002 Nobel Prize in Chemistry

Applications of NMR

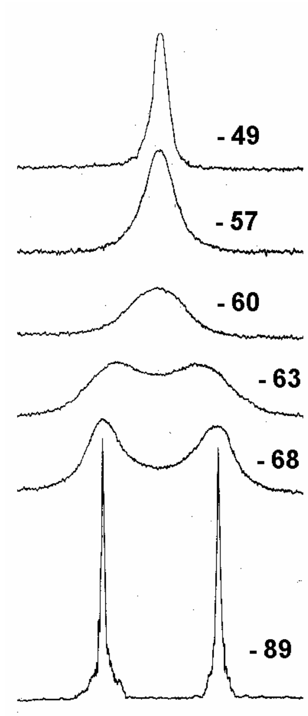
HPLC-NMR / MS

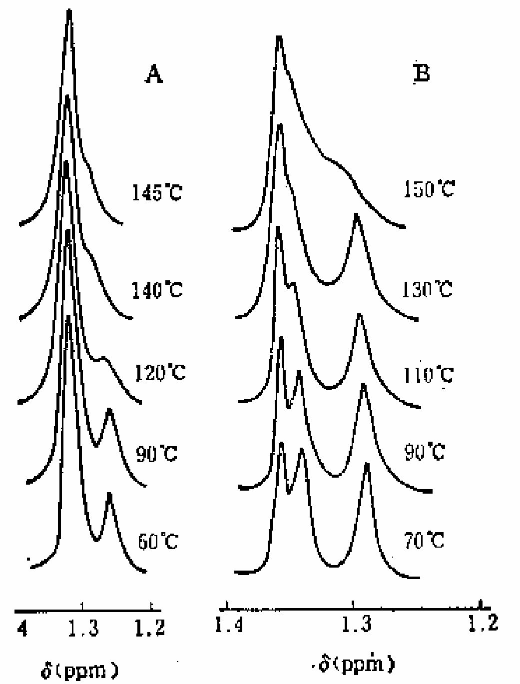


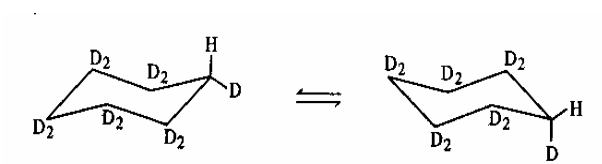


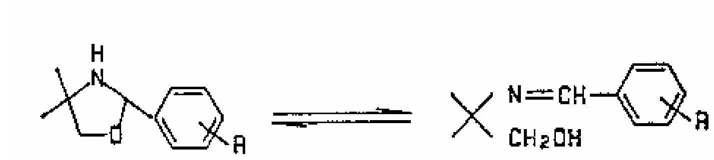
Applications of NMR

Dynamic NMR (DNMR)







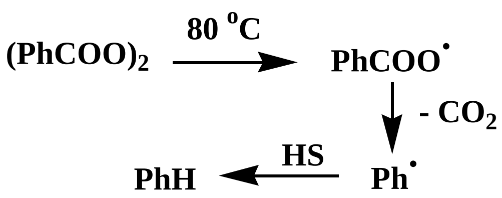


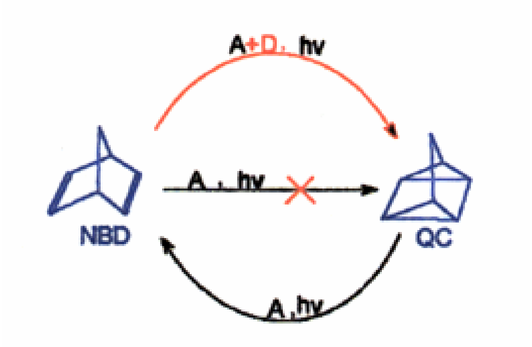
Inversion Barrier ~ 10 kcal / mol

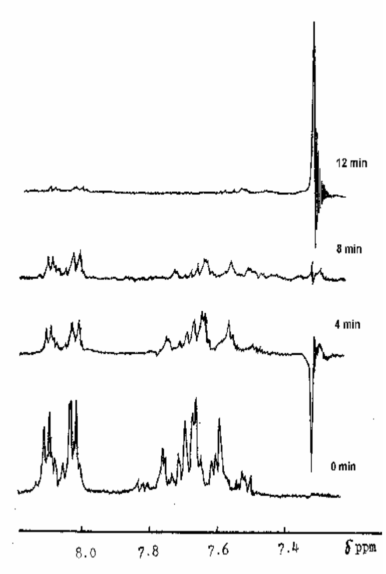
Inversion Barrier ~ 21 kcal / mol
Yang, Chen. J. Chem., 1990, 428

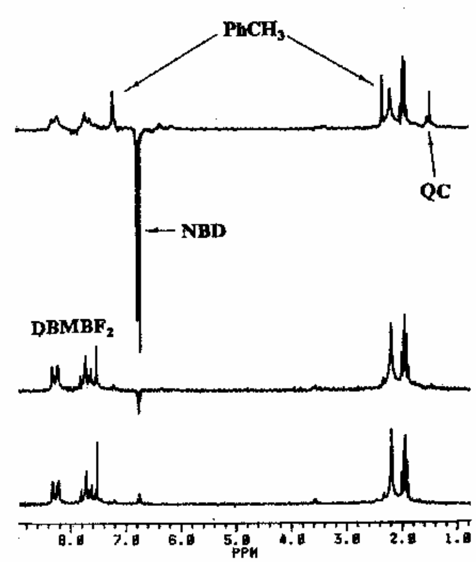
Applications of NMR

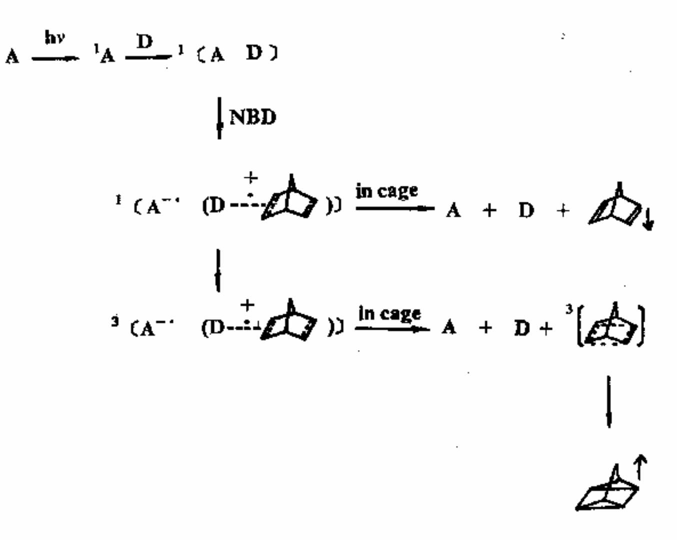
Chemically Induced Dynamic Nuclear Polarization (CIDNP)









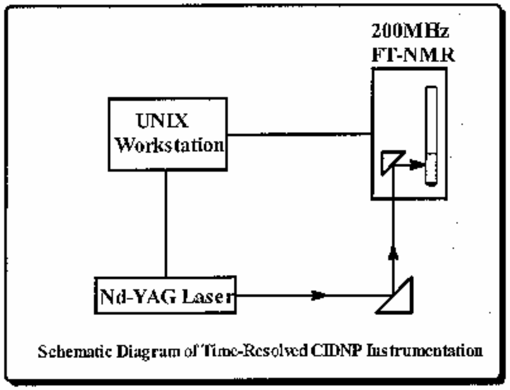


Fischer, 1967

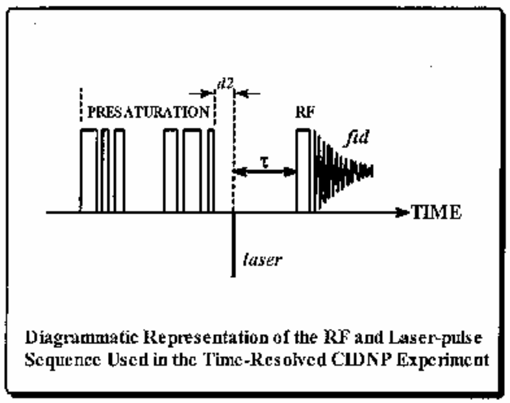
Yang, et al., JCS Perkin 2, 1994, 585
ChemComm., 1996, 451

Applications of NMR

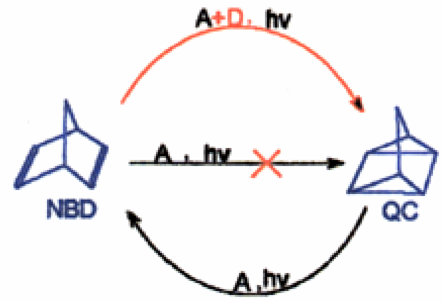
Time-Resolved CIDNP

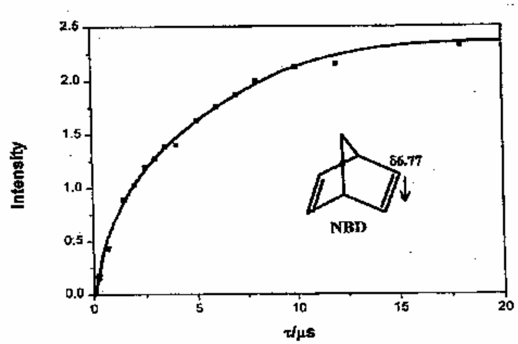


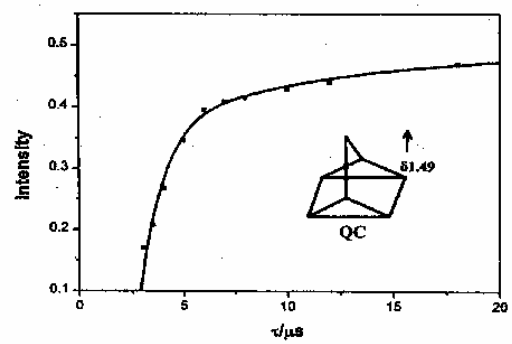
Schematic Diagram of Time-Resolved CIDNP Instrumentation



Diagrammatic Representation of the RF and Laser-pulse Sequence Used in the Time-Resolved CIDNP Experiment







Yang, Gomberg 2000, 2000

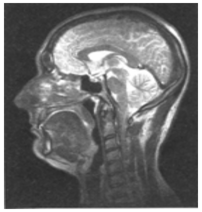
Applications of NMR

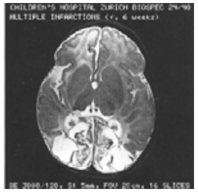
NMR Imaging (MRI)

P. Lauterbur
P. Mansfield

2003 Nobel Prize in Medicine



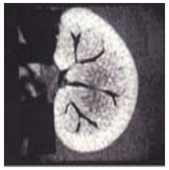




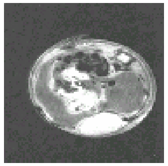


NMR Microscopy

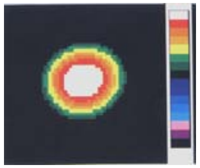








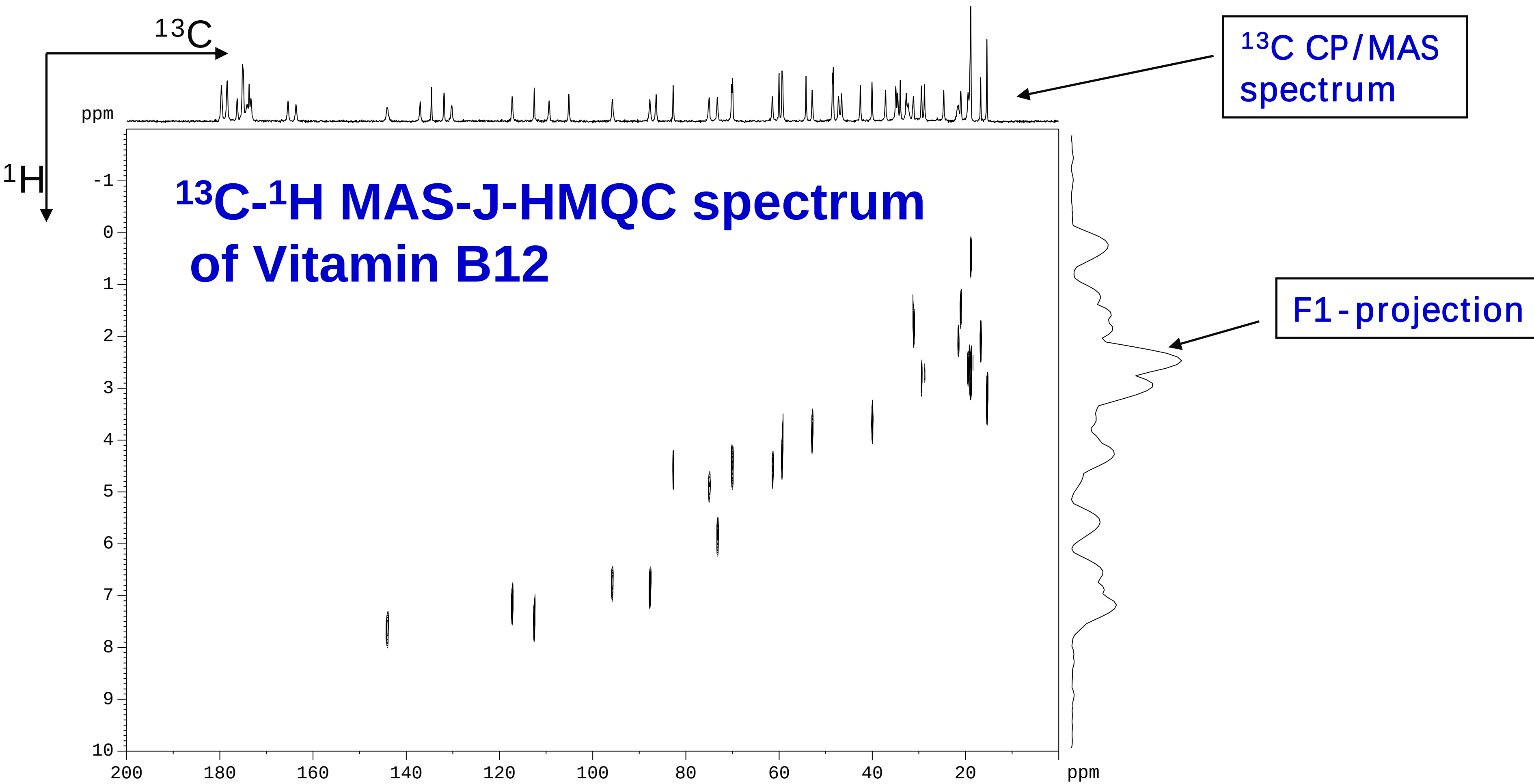






Applications of NMR

High Resolution NMR in the Solid State

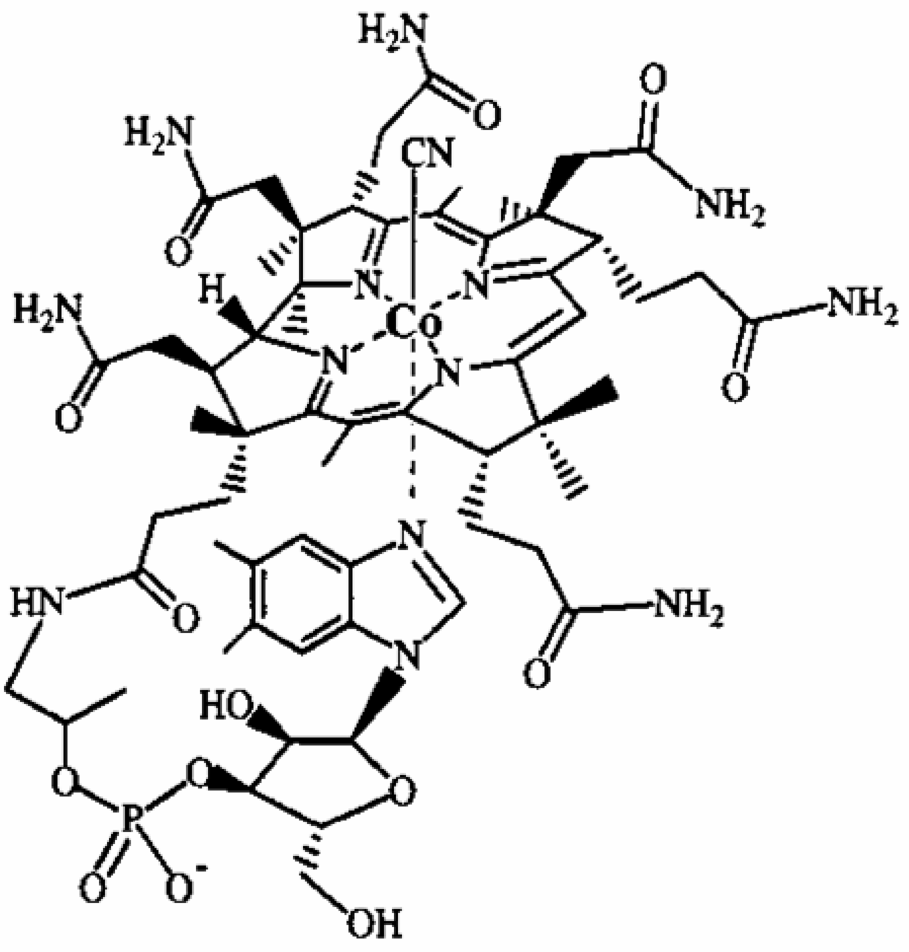


400 MHz spectrometer, spinning speed 13,717 kHz, contact time 1 ms

Applications of NMR

High Resolution NMR in the Solid State

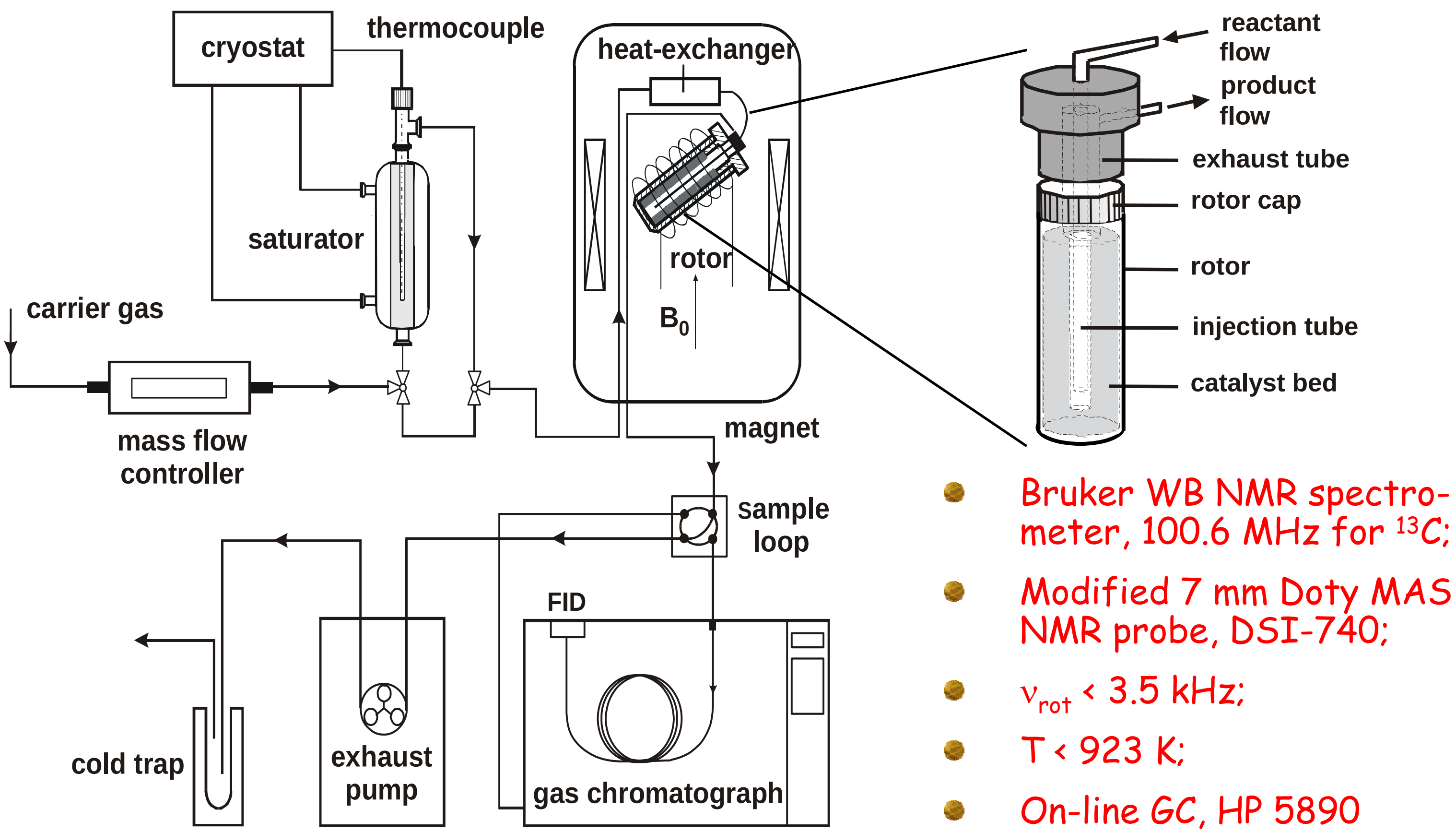
Vitamin B_{12}
$C_{63}H_{88}CoN_{14}O_{14}P$



Vitamin B_{12}

Applications of NMR

In Situ MAS (magic-angle-spinning)NMR in the Solid State



- Bruker WB NMR spectrometer, 100.6 MHz for ^{13}C;
- Modified 7 mm Doty MAS NMR probe, DSI-740;
- ν_{rot} < 3.5 kHz;
- T < 923 K;
- On-line GC, HP 5890

In last course, we were talking about…

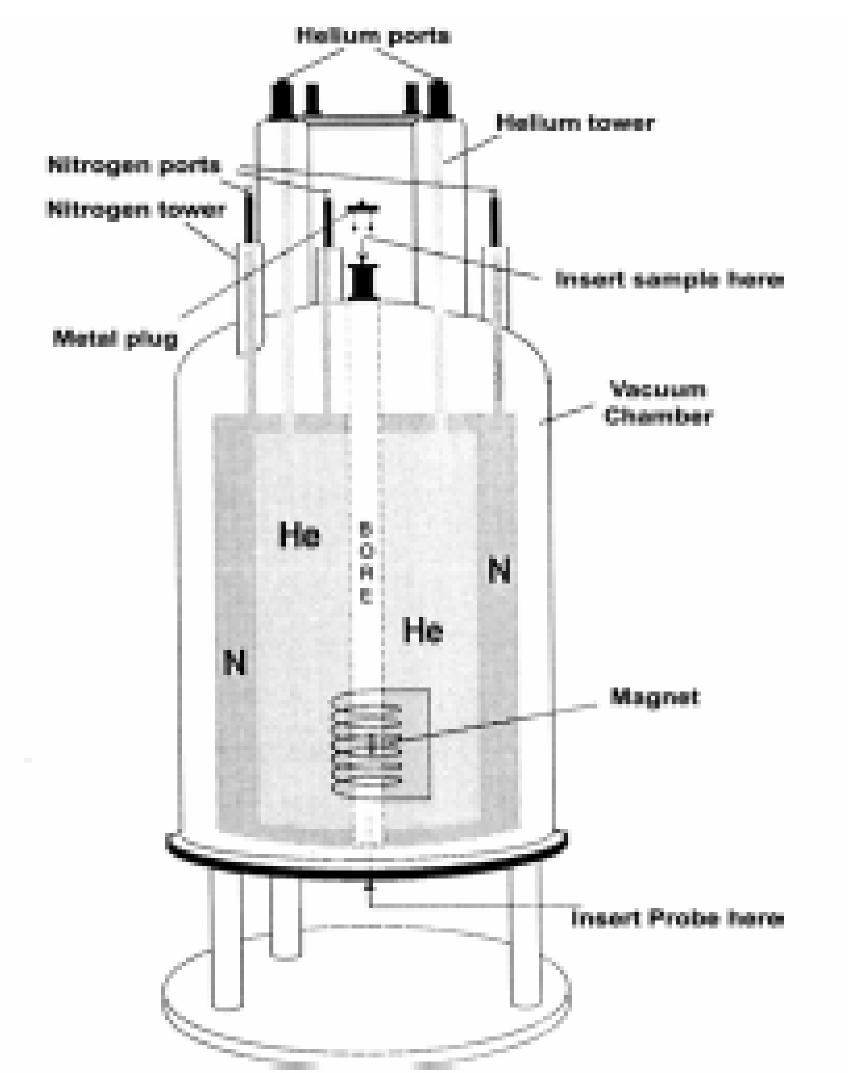
In last course, we were talking about…

- NMR history
- NMR spectrometer: structure, magnet, probe
- NMR safety
- Applications of NMR spectroscopy

NMR Spectrometer

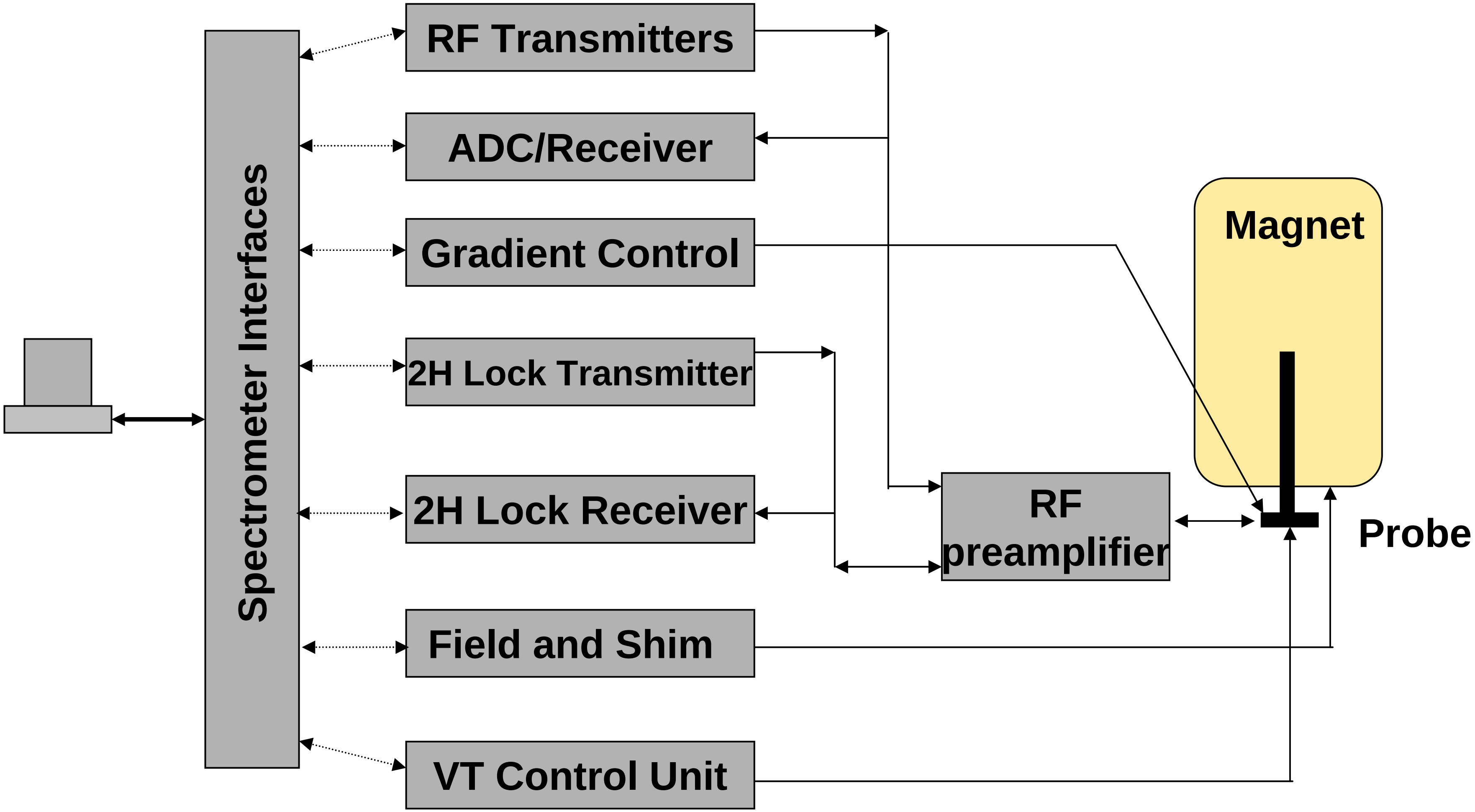
- **Superconducting magnet**
- **Probe**
- **Console (rf mixers, amplifiers, locking system, gradients, shim power supply, etc.)**
- **Host and acquisition computer**

Superconducting Magnet

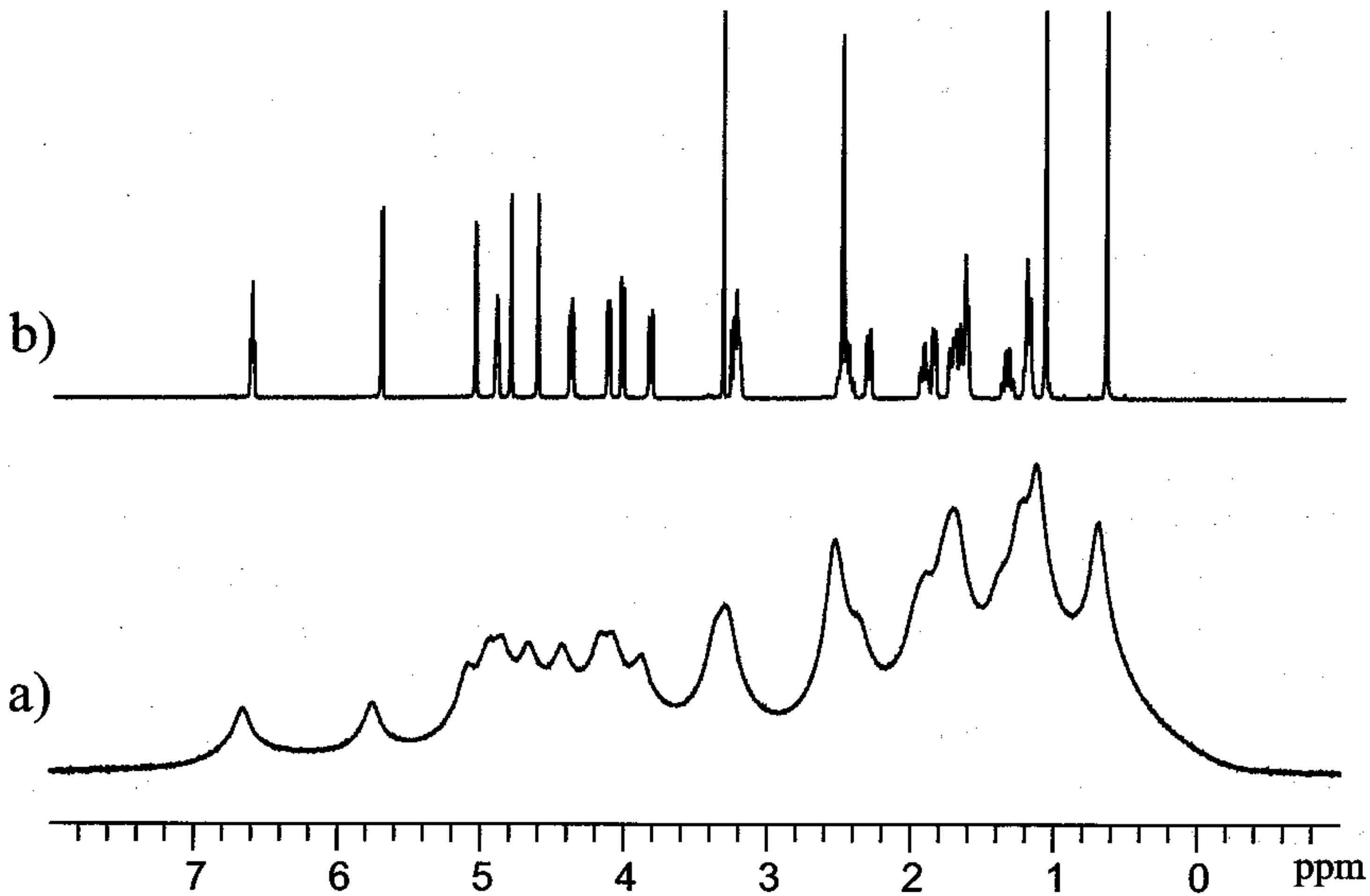




Spectrometer Console



Optimizing Field Homogeneity - Shimming



Chapter 1: Basic Principles of NMR

- Nuclear Spin
- Nuclear Magnetic Resonance
- The Vector Model
- Pulsed Fourier-Transform NMR
- Relaxation

Structure of Atomic Nucleus

- Atomic nucleus consists of neutrons and protons
- An atomic nucleus is specified by atomic number, mass number, and spin quantum number
- **Atomic number** specifies number of protons of the nucleus [chemical symbol: H(Z=1), C(Z=6), N(Z=7)]
- **Mass number** specifies number of neutrons of the nucleus
- **Isotope:** nuclei with the same atomic number, but different mass number. For example: $^{1}H = p$, $^{2}H = p + n$ and $^{12}C = 6p + 6n$, $^{13}C = 6p + 7n$

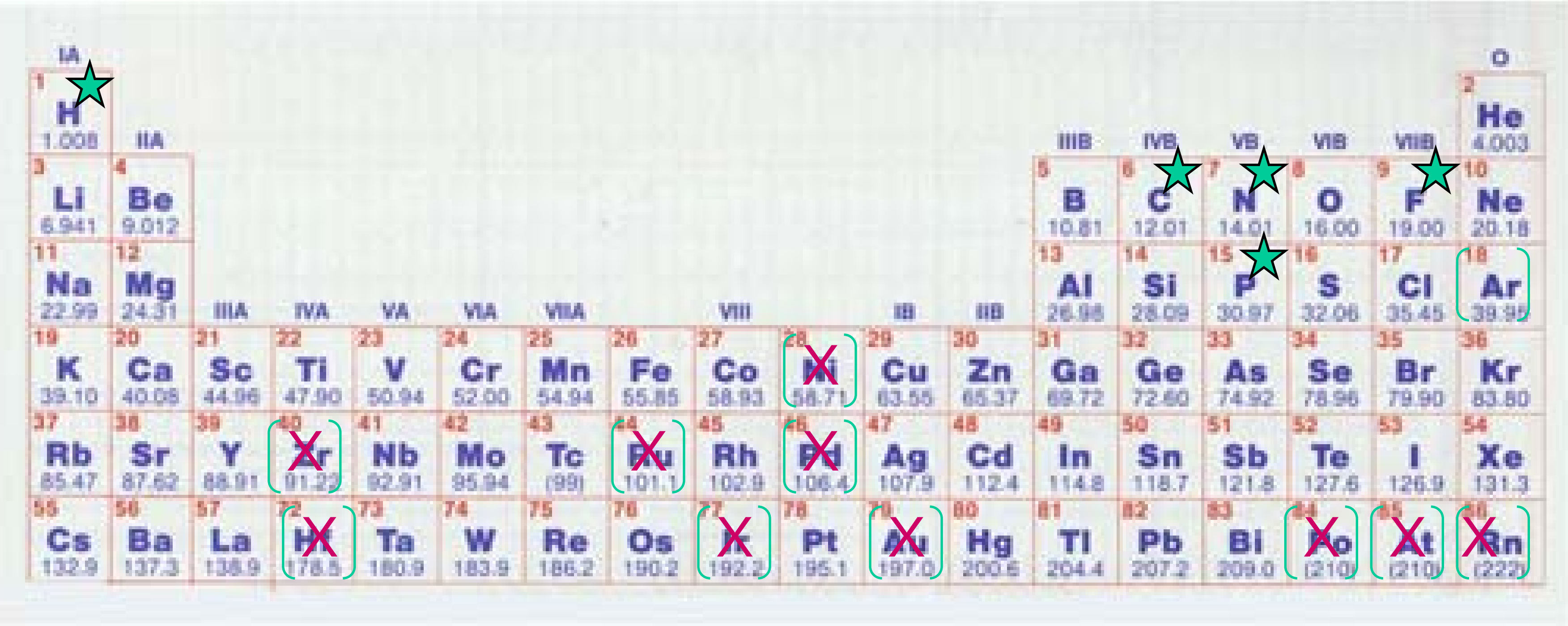
Nuclear Spin

- **<u>Nuclear spin quantum number (*I*)</u>** specifies nuclear spin, which is a fundamental and *intrinsic* property of atomic nucleus
- Suggested by Pauli in 1924 to explain hyper-structure of atomic spectra
- The hyper-structure or splittings of atomic spectroscopy in the inhomogeneous magnetic fields demonstrated that nuclei of diffident elements (and different isotopes of of the same element) differ in spin angular momentum

Nuclear Spin Quantum Number (I)

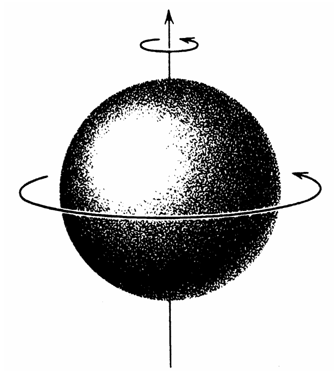
I	Atomic Mass	Atomic Number	Example (I)
Half-integer	Odd	Odd or even	$^{1}_{1}H(\frac{1}{2})$, $^{17}_{8}O(\frac{5}{2})$, $^{15}_{7}N(\frac{1}{2})$
Integer	Even	Odd	$^{2}_{1}H(1)$, $^{14}_{7}N(1)$, $^{10}_{5}B(3)$
Zero	Even	Even	$^{12}_{6}C(0)$, $^{16}_{8}O(0)$, $^{34}_{16}S(0)$

NMR Periodic Table of Elements



$I \neq 0$

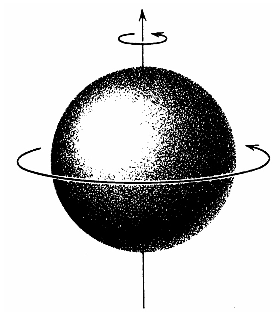
Nuclear Magnetic Moment (μ) and Nuclear Spin (I)



$$\mu = \frac{\gamma I h}{2\pi}$$

μ: **nuclear magnetic moment**
I: **nuclear spin quantum number**
γ: **magnetogyric ratio or gyromagnetic ratio**
h: **Planck constant**

Nuclear Magnetic Moment (μ) and nuclear spin (I)



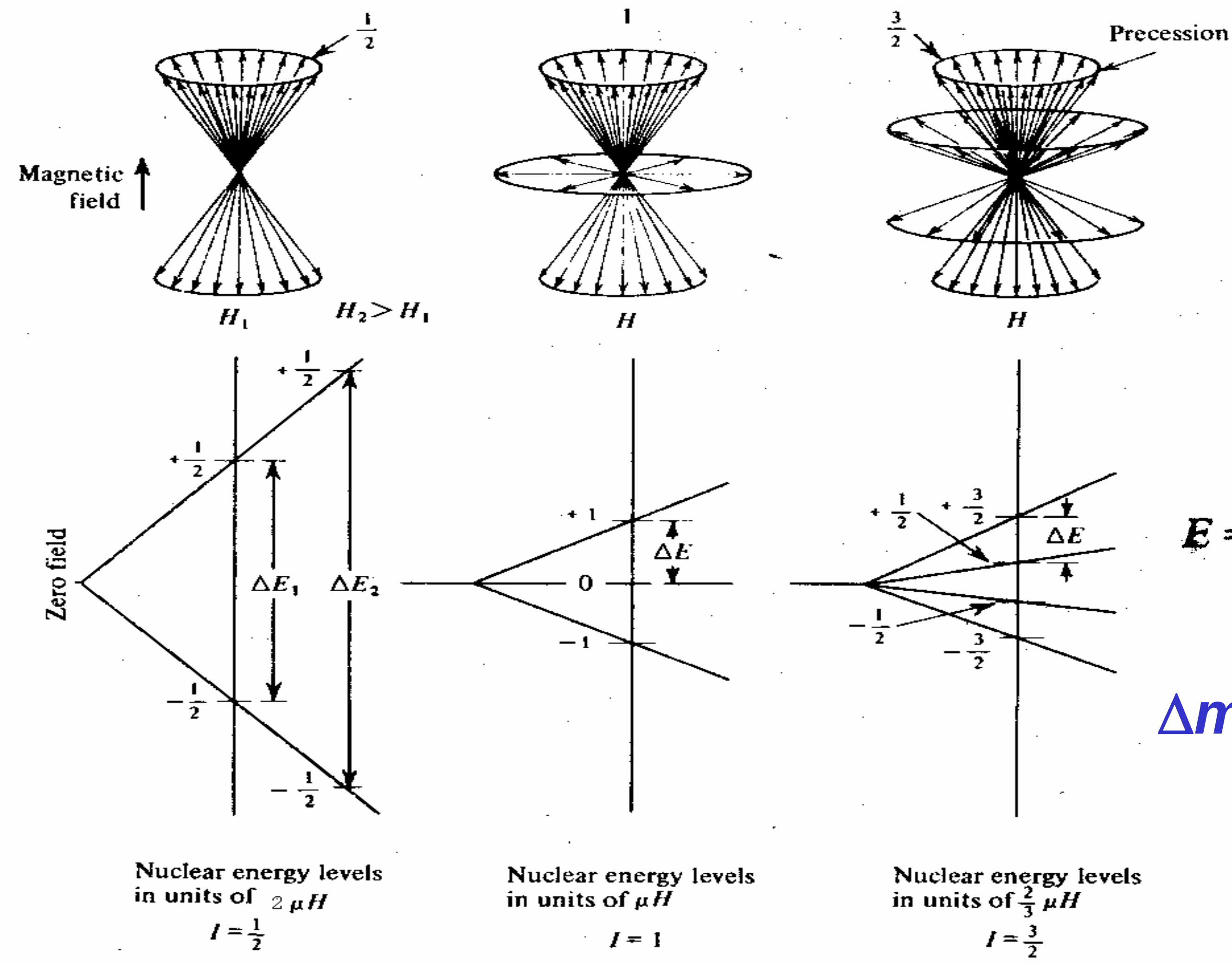
$$\mu = \frac{\gamma I h}{2\pi}$$

when a static magnetic field is applied…

$$E = -\frac{\gamma h}{2\pi} m_I B$$

m_I: magnetic quantum number,
has the values of $-I$, $-I + 1$,.., $I - 1$, I
B: the applied magnetic field

Nuclear Orientation and Energy Levels in a Static Magnetic Field (*H*)



$$E = -\frac{\gamma h}{2\pi} m_I B$$

$$\Delta m_I = \pm 1$$

NMR is an Insensitive Method

$$\Delta E = E_{\alpha} - E_{\beta} = \eta\omega = \eta\gamma B_{0}$$

$$\text{NMR signal} \propto (N_{\alpha} - N_{\beta})$$

$$\frac{N_{\beta}}{N_{\alpha}} = e^{-\Delta E / kT}, \qquad N_{\beta} = N_{\alpha} e^{-\Delta E / kT}$$

$$(N_{\alpha} - N_{\beta}) = N_{\alpha} - N_{\alpha} e^{-\Delta E / kT} = N_{\alpha}(1 - e^{-\Delta E / kT})$$

For a 500 MHz NMR at 300 K,

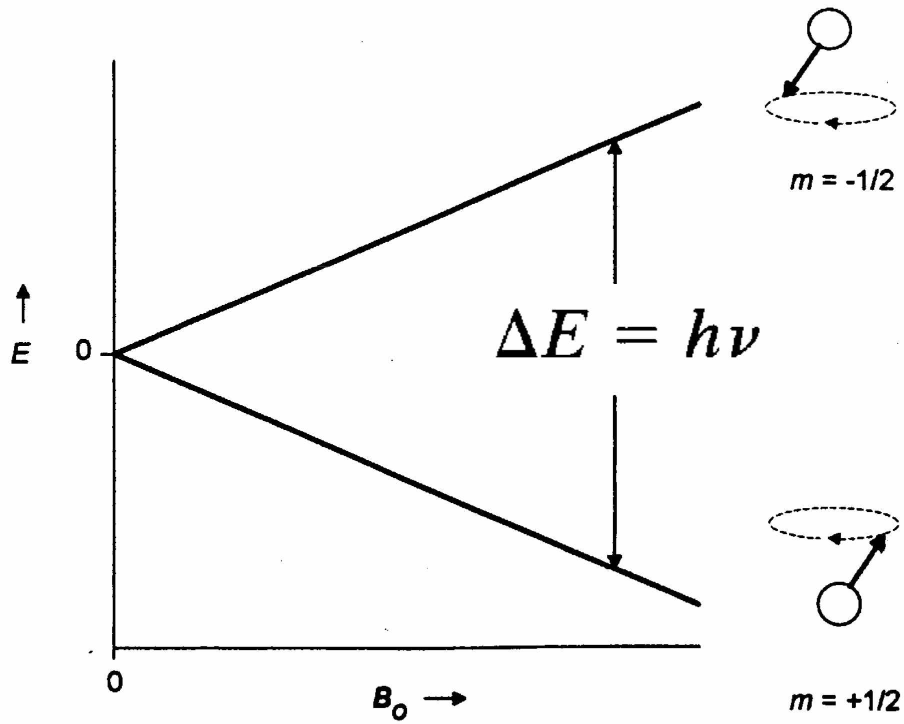
$$\Delta \mathrm{E} = 1.054 \times 10^{-34}\,\mathrm{Js} \cdot 2.67519 \times 10^{8}\,\mathrm{radT}^{-1}\mathrm{s}^{-1} \times 11.74\mathrm{T} = 3.31 \times 10^{-25}\,\mathrm{J}$$

$$\text{Therefore } (1 - e^{-\Delta E / kT}) \approx 8.0 \times 10^{-5} \text{ or } \Delta \mathrm{N} = 8.0 \times 10^{-5} \cdot N_{\alpha}$$

If one million molecules is under consideration,

$$N_{\alpha} = 500020 \text{ and } N_{\beta} = 499980 \quad \Delta N = 40$$

NMR Resonance Condition



Relative energy of both spin states of an $I = \frac{1}{2}$ nucleus as a function of the strength of the external magnetic field $\mathbf{B}_0$.

$$E_i = -m_i \frac{\gamma h \mathbf{B}_0}{2\pi}$$

$\Delta m_I = \pm 1$, therefore…

$$\Delta E = E_{(m=-1/2)} - E_{(m=1/2)}$$

$$\Delta E = \frac{h\gamma}{2\pi} \boldsymbol{B}_0$$

On the other hand…

$$\Delta E = h\nu$$

$$\nu = \gamma \mathbf{B}_0 / 2\pi$$

Unit in NMR

$$\omega = -\gamma B_0 \,\mathrm{rad\,s^{-1}} \qquad \upsilon = -\frac{\gamma B_0}{2\pi}$$

where B_0 is magnetic field strength in Tesla.

For a 500 MHz NMR spectrometer,

$$B_0 = -\frac{2\pi \cdot 500 \times 10^6\,\mathrm{s^{-1}}}{26.7519 \times 10^7\ \mathrm{rad\ T^{-1}s^{-1}}} = 11.74\,(\mathrm{Tesla})$$

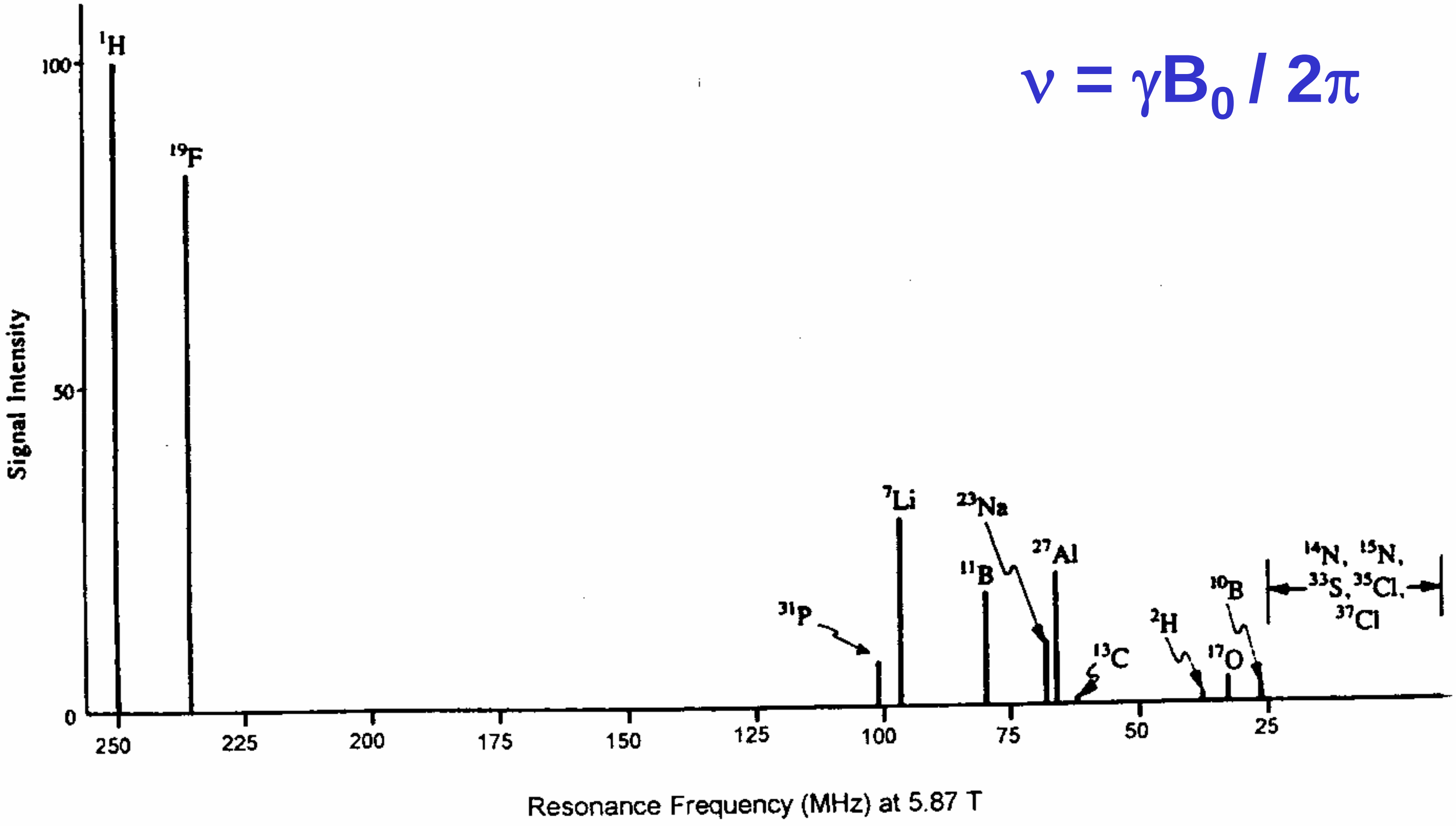
With B_0 of 11.7 Tesla, ^{13}C NMR frequency,

$$\upsilon = -\frac{6.7283 \times 10^7\,\mathrm{rad\ T^{-1}\,s^{-1}} \cdot 11.74\,\mathrm{T}}{2\pi} = -125.7 \times 10^6\,\mathrm{Hz}$$

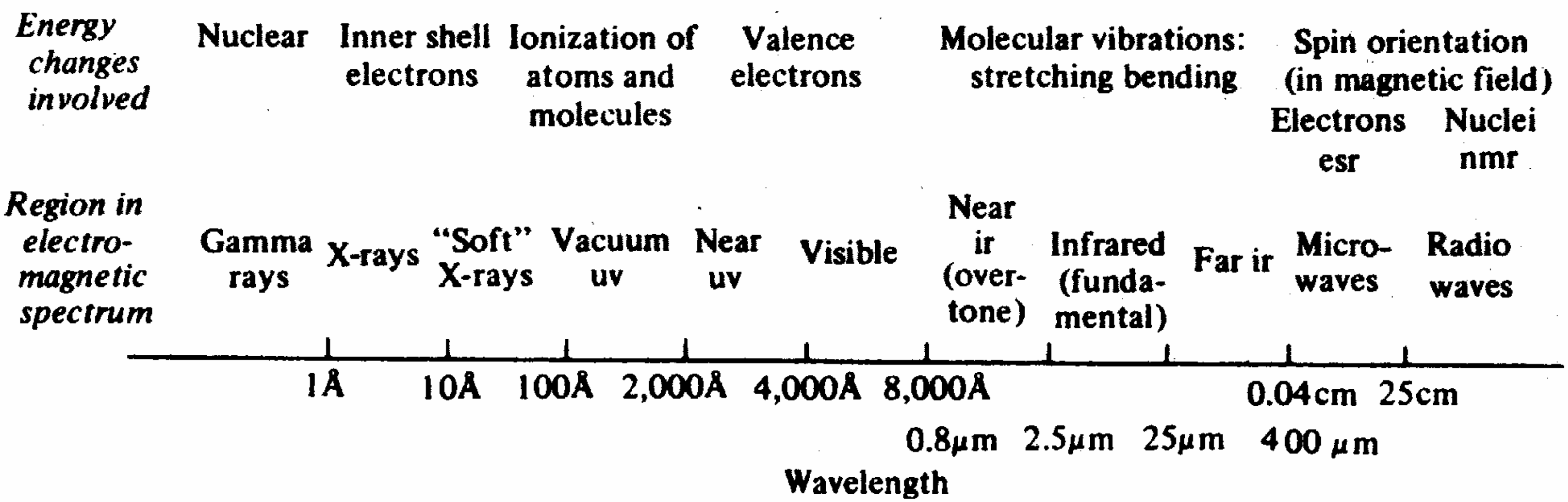
$$= -125.7\,\mathrm{MHz}$$

Resonance Frequencies of Common Nucleus (5.87 T)

$$\nu = \gamma B_0 / 2\pi$$



NMR Frequency

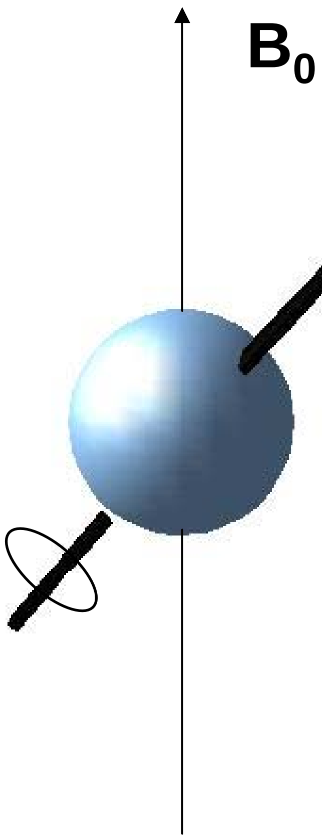


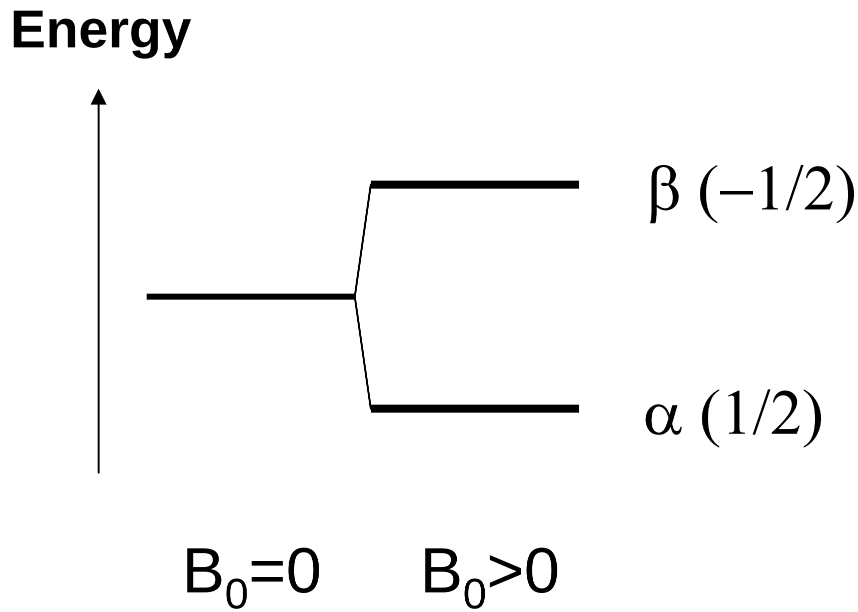
Schematic diagram of electromagnetic spectrum

The Vector Model

- **The vector model provides a sort of simple, intuitive, non-mathematical picture of total magnetization and its precession, and its movement under the influence of r.f. pulse.**
- **It is limited to an isolated system of spin-1/2 nuclei. It does not work for "coupled-spin" system and other more complex NMR experiments.**

For Nuclear Spin of I = 1/2

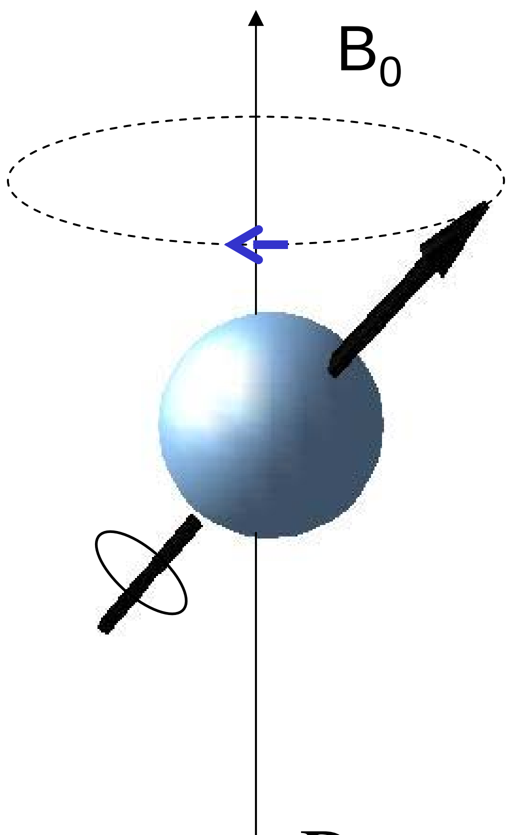




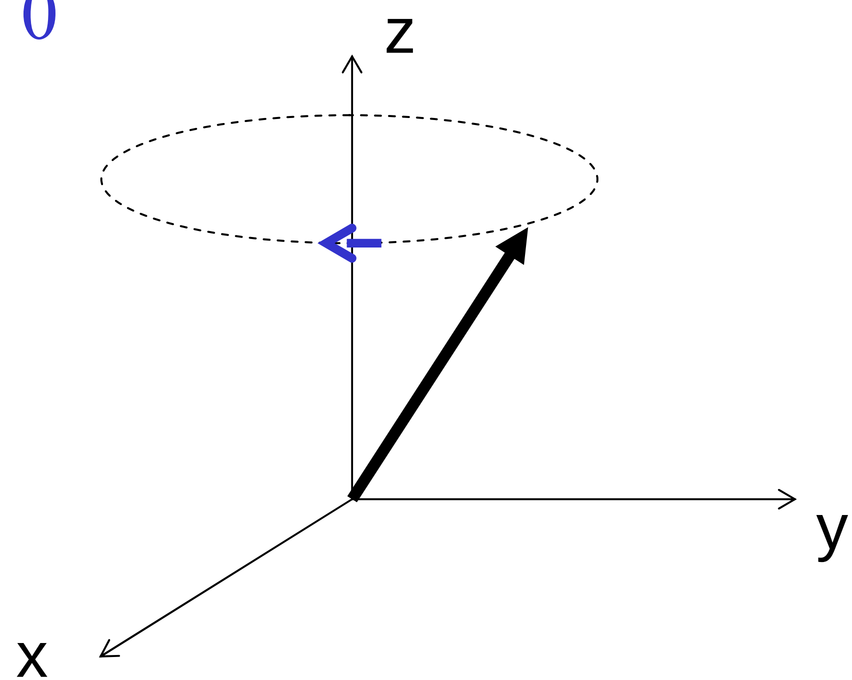
Spin I = 1/2

^{1}H, ^{13}C, ^{19}F, ^{15}N, and ^{31}P

Nuclear Spin and Resonance



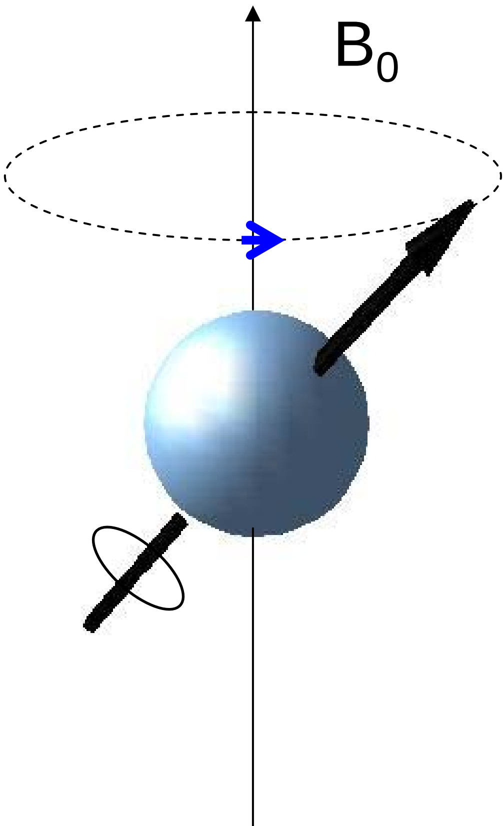
$\gamma > 0$

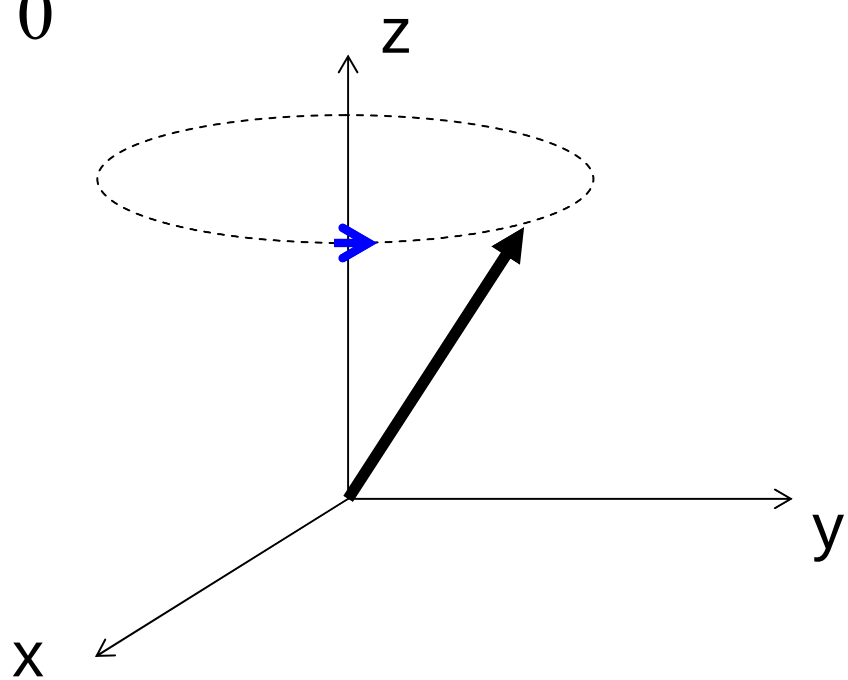


$$\mu = \gamma P \qquad \omega = -\gamma B_0 \ \mathrm{rad\,s^{-1}} \qquad \upsilon = -\frac{\gamma B_0}{2\pi}\ \mathrm{Hz}$$

Nuclear Spin and Resonance

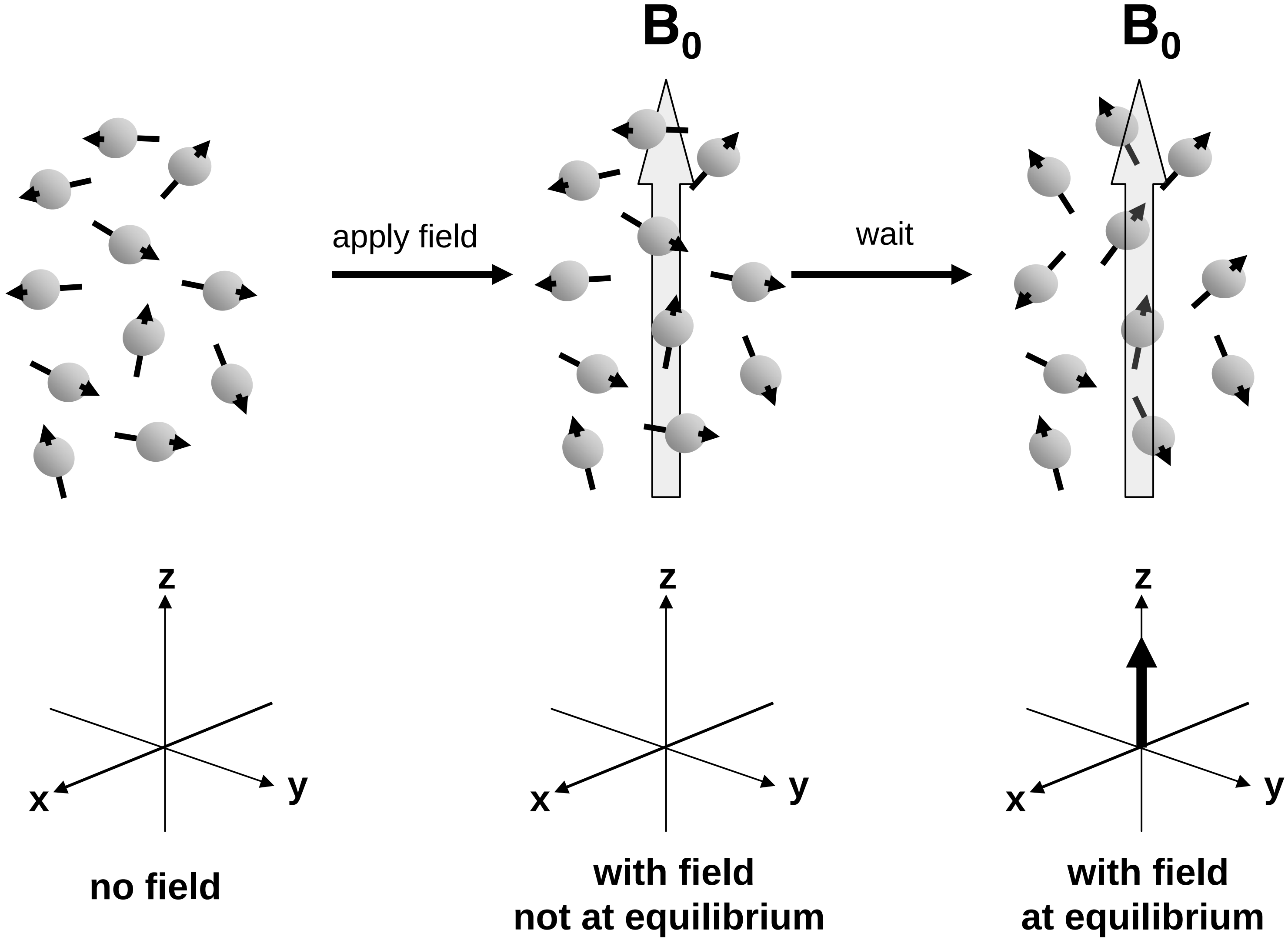
$\gamma < 0$



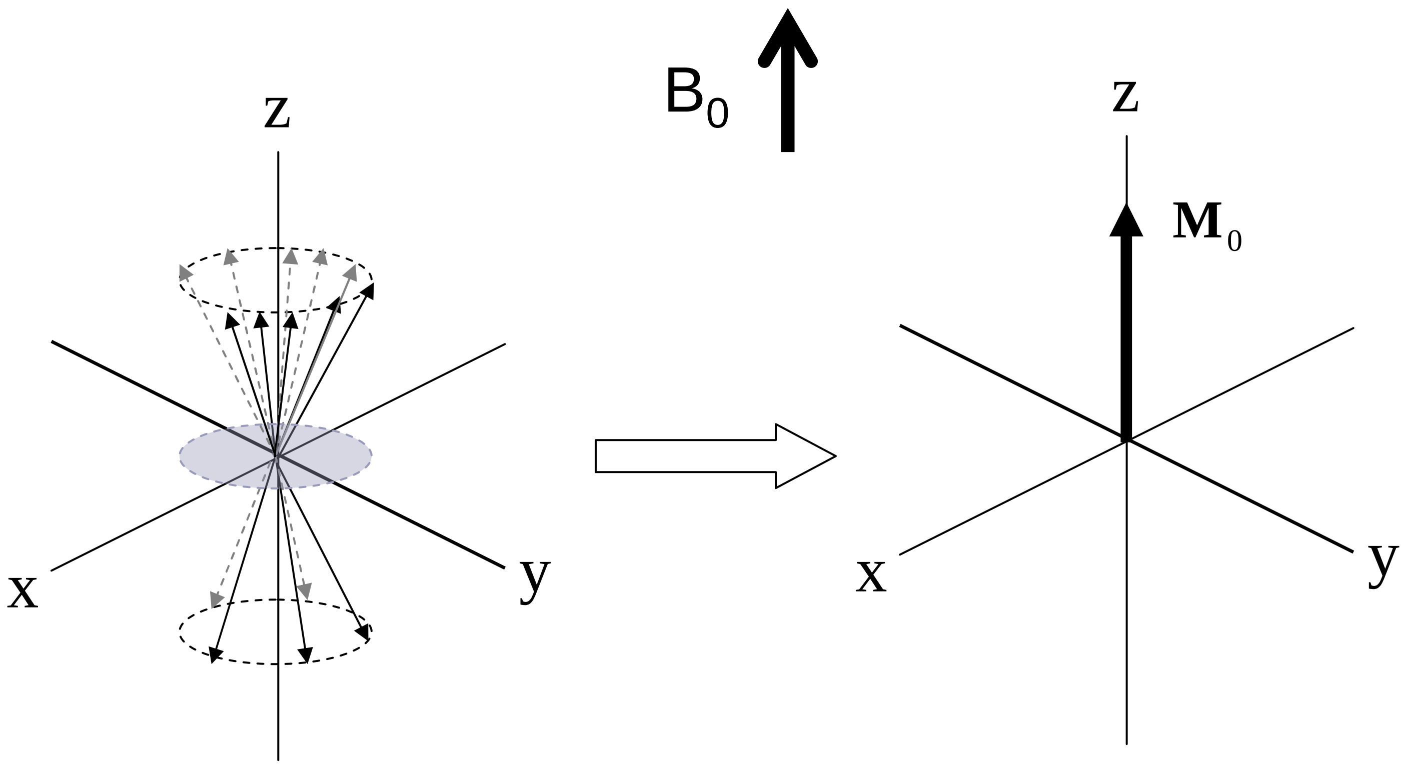


$\mu = \gamma P$ $\quad \omega = -\gamma B_0 \text{ rad s}^{-1}$ $\quad \upsilon = -\frac{\gamma B_0}{2\pi} \text{ Hz}$

Vector Model - A Collection of Spins

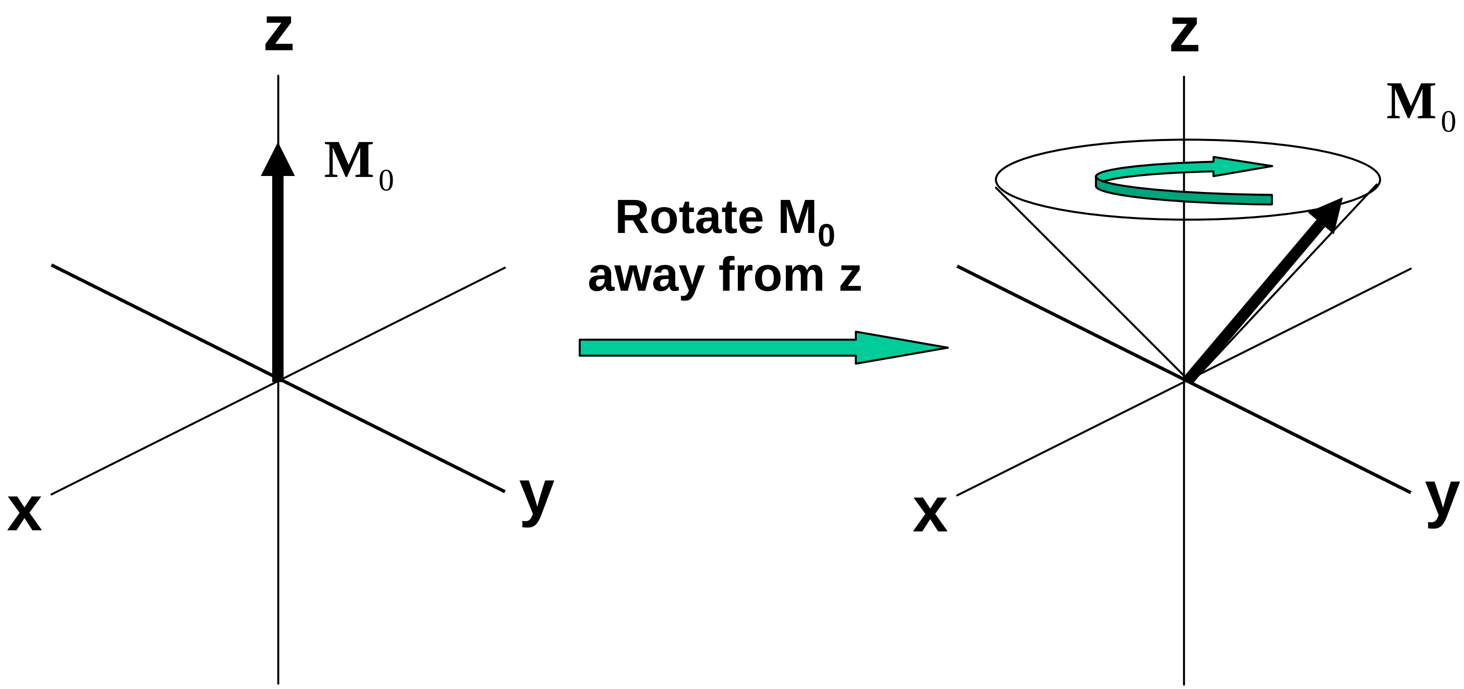


Magnetization - Longitudinal



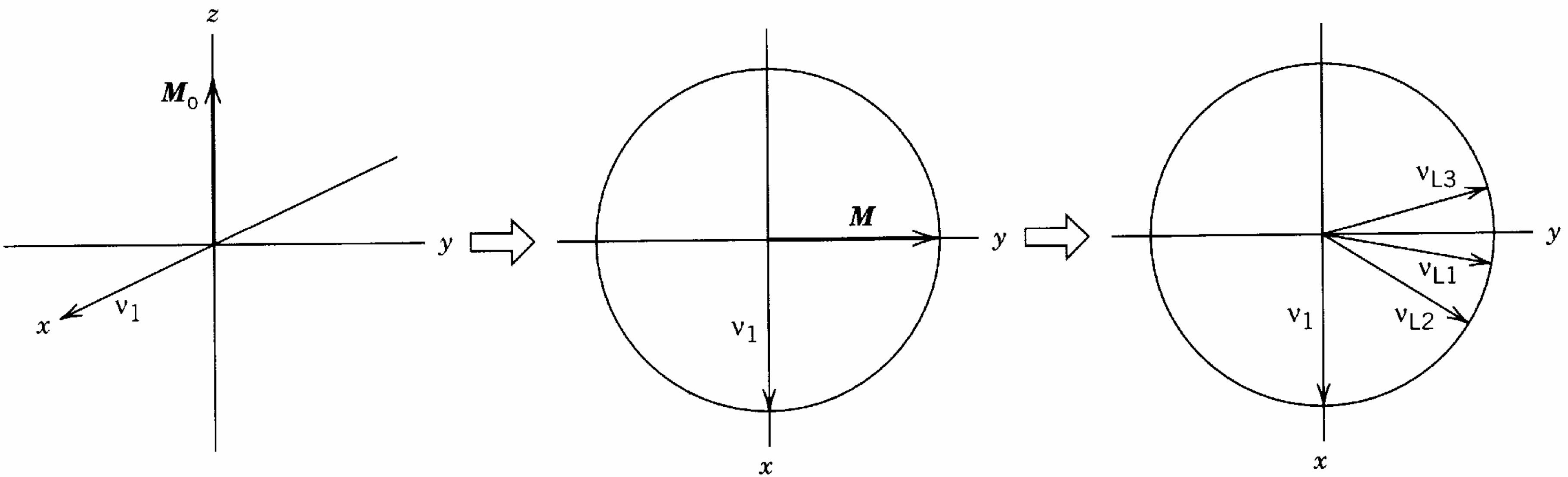
The equilibrium magnetization is longitudinal and usually not observable! Only the transverse magnetization is measurable.

Magnetization - Larmor Precession



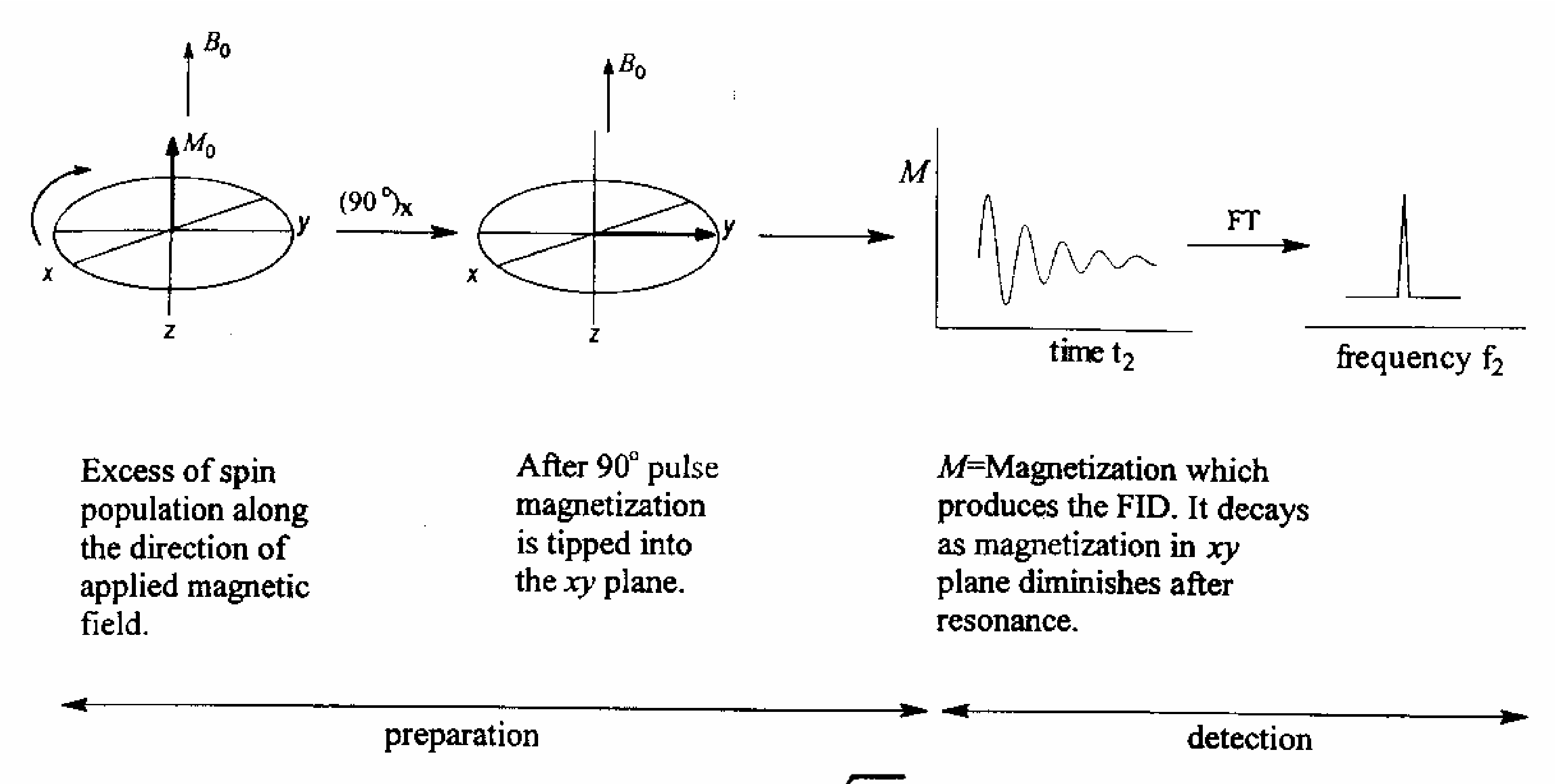
$$\omega_0 = -\gamma B_0 \text{ in rad s}^{-1}$$

Pulsed Fourier Transform (PFT)-NMR



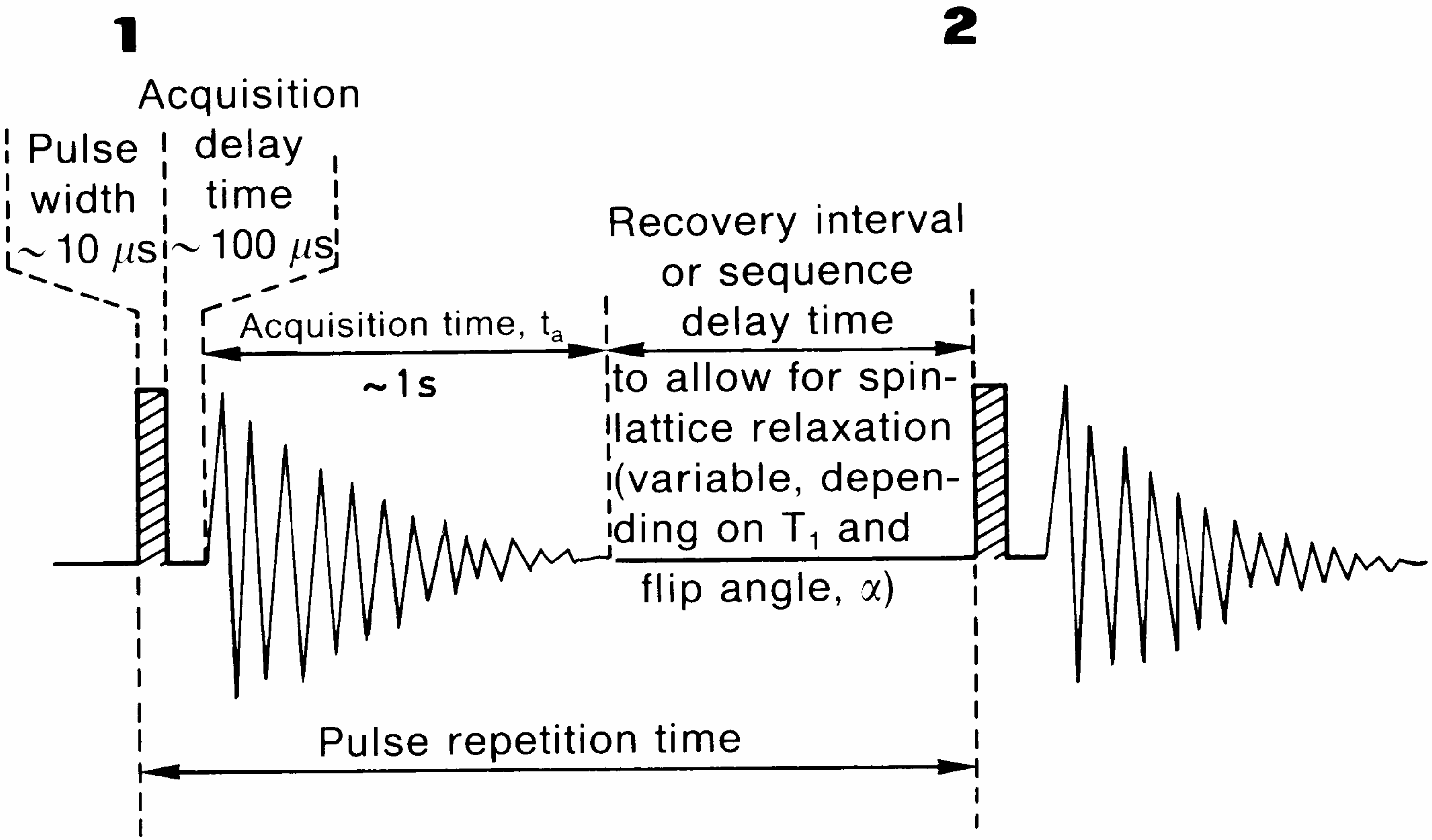
A rotating frame of reference. The net magnetization **M** (following a 90° pulse) has three components with Larmor frequencies ν_{L1}, ν_{L2}, and ν_{L3} (i.e., three different protons). The frame is rotating at ν_1 (the applied pulse). Immediately following the pulse, the components are precessing *relative* to ν_1: ν_{L1} and ν_{L2} have higher frequencies than the frequency of the applied pulse ν_1, but the frequency of ν_{L3} is lower than that of ν_1.

Mechanism of Pulsed FT-NMR

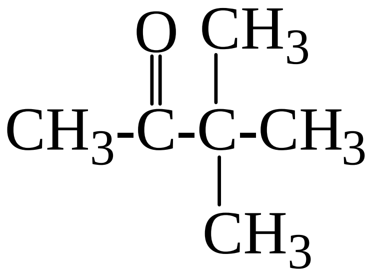


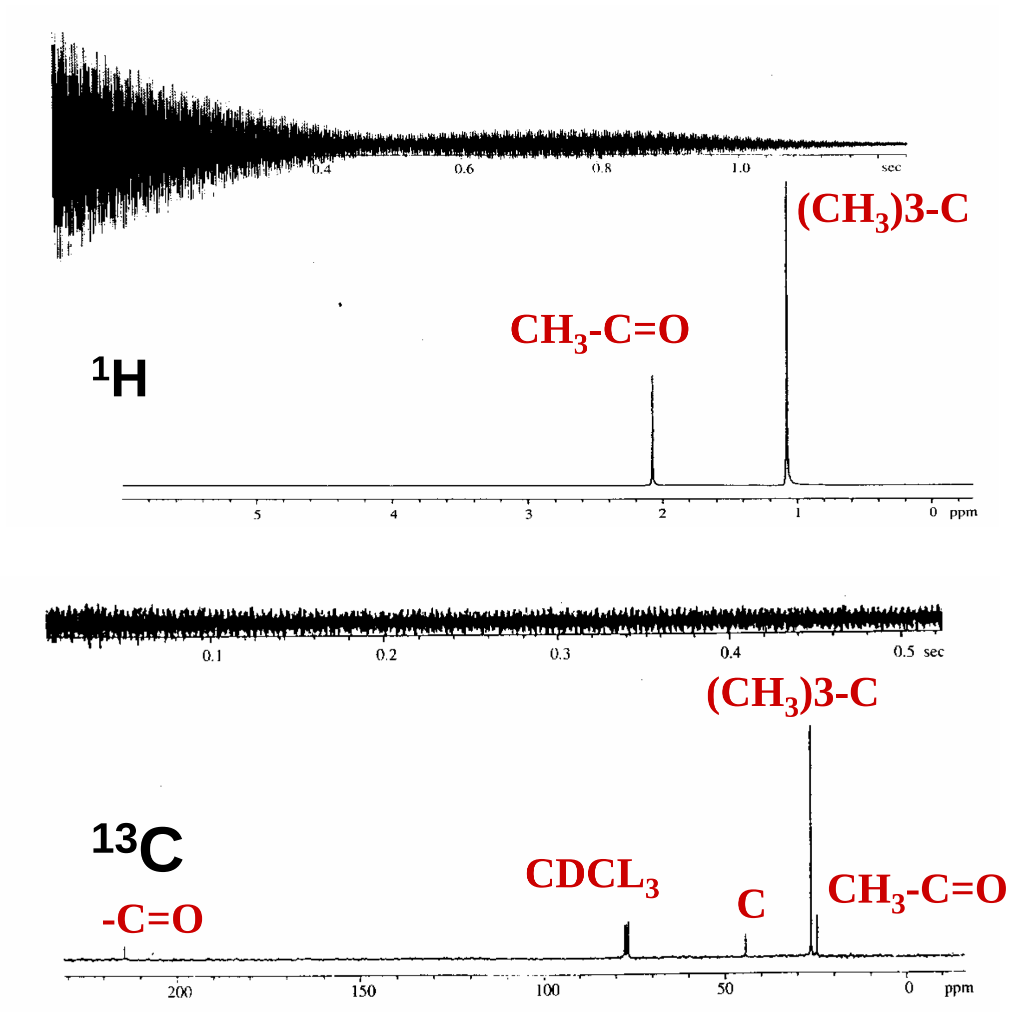
$$S/N \propto \sqrt{N}$$

Pulsed FT-NMR



Relationship between Free Induction Decay (FID) and Frequency Spectrum in PFT NMR





Most Important 1D NMR Parameters

^{1}H NMR: Chemical shift (δ)

Coupling constant ($J_{H\text{-}H}$)

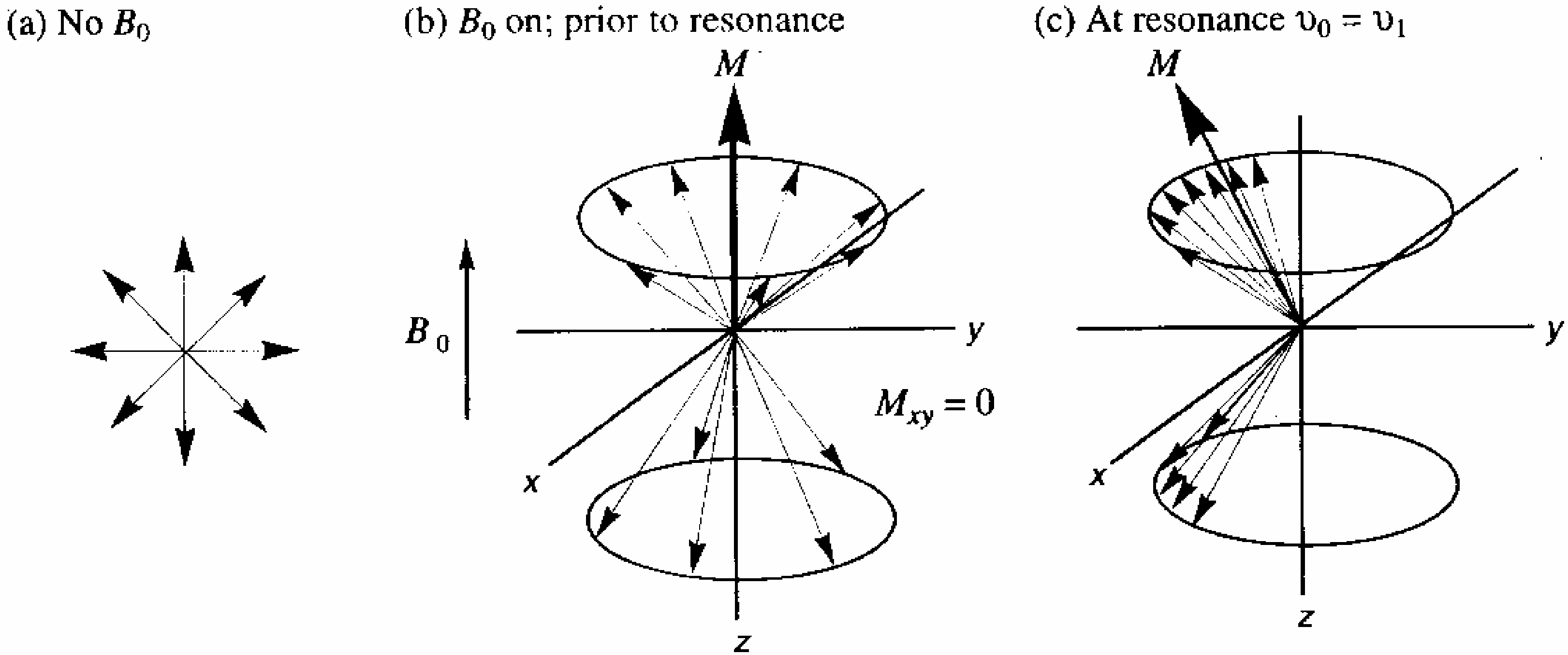
Integration area (Number of protons)

^{13}C NMR: Chemical shift (δ)

Coupling constant ($J_{C\text{-}H}$)

Relaxation time

Magnetization Changes along z and xy Plane

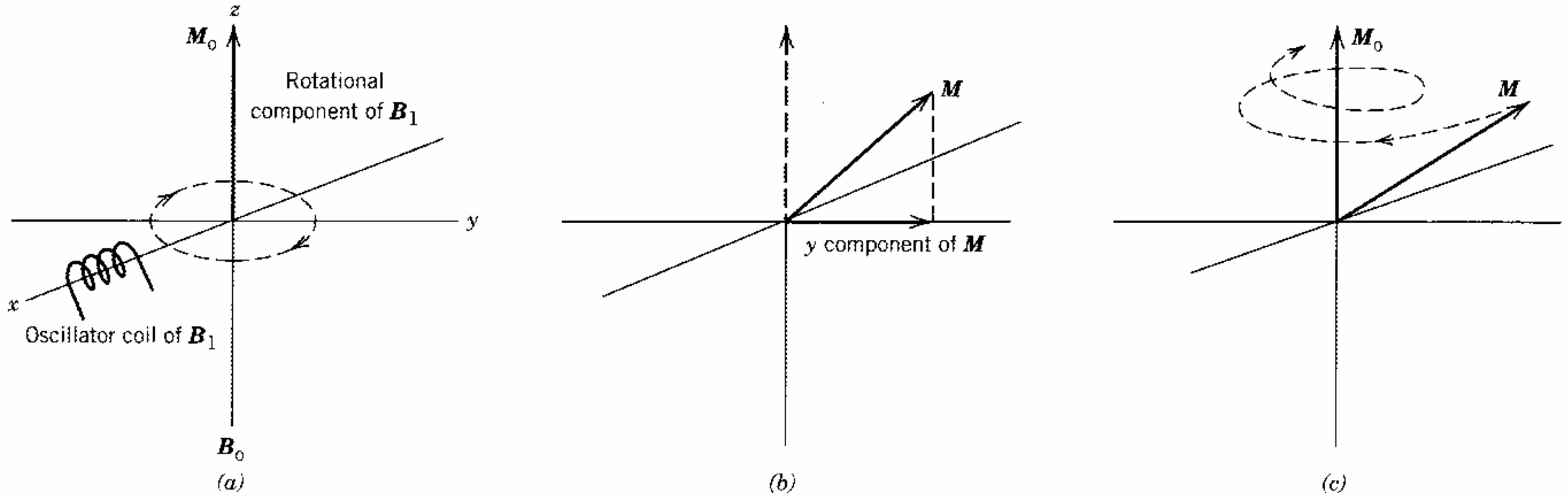


Random orientation of magnetic dipoles.

Net polarization M (or M_z) along the z axis is due to population excess in lower energy state. The magnetic vectors precess about B_0 at the Larmor frequency υ_0.

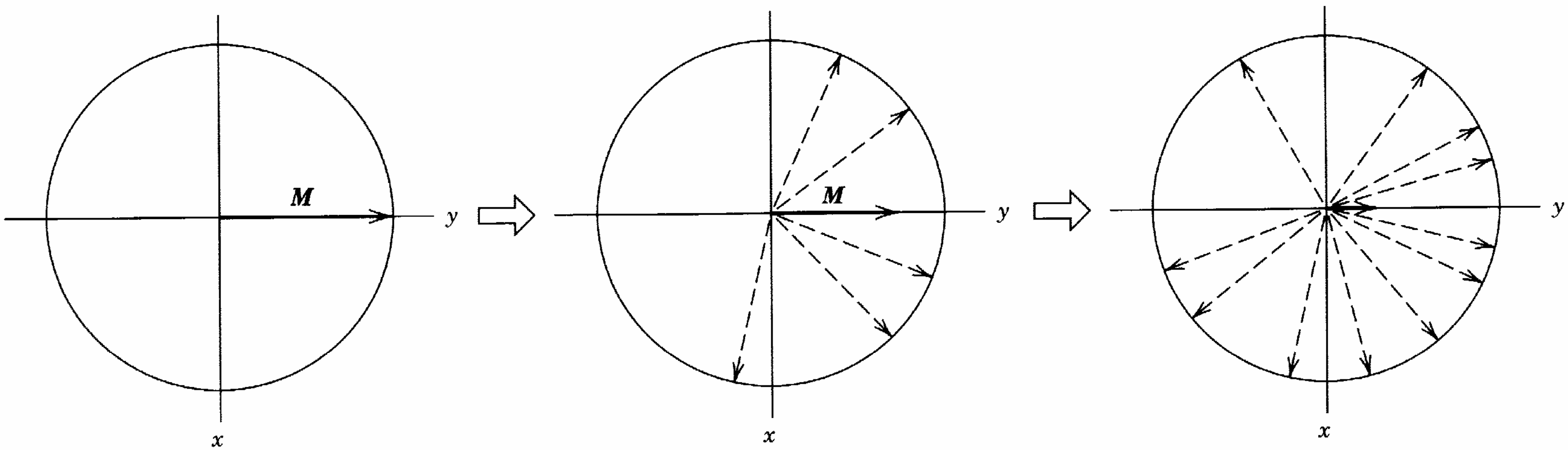
The magnetic vectors precess in phase with frequency υ_1.
After resonance, the return to the equilibrium in (b) occurs by the loss of M_{xy} via dephasing of nuclear dipoles by T_2 and increase in M_z by spin inversion due to T_1.

Spin-Lattice Relaxation (T_1)



Oscillator generates rotating component of applied magnetic field $\boldsymbol{B}_1$. The net magnetization $\mathbf{M}_0$ is tipped to $\mathbf{M}$, which precesses about the z axis generating a component of magnetization in the horizontal plane. (c) Longitudinal relaxation of $\mathbf{M}$ to $\mathbf{M}_0$ follows a decreasing spiral. Transverse relaxation T_2 (dephasing of $\mathbf{M}$) is omitted. The Cartesian frame is stationary.

Spin-Spin Relaxation (T_2)



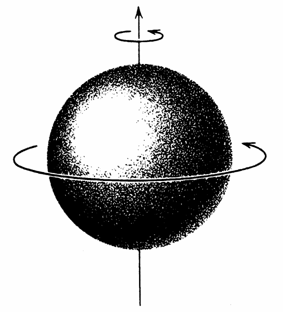
T_2 relaxation in the xy plane of a rotating frame.

In last course, we were talking about…

In last course, we were talking about…

- **Nuclear Spin**
- **Nuclear Magnetic Resonance**
- **The Vector Model**
- **Pulsed Fourier-Transform NMR**
- **Relaxation**

Nuclear Magnetic Moment (μ) and Nuclear Spin (I)



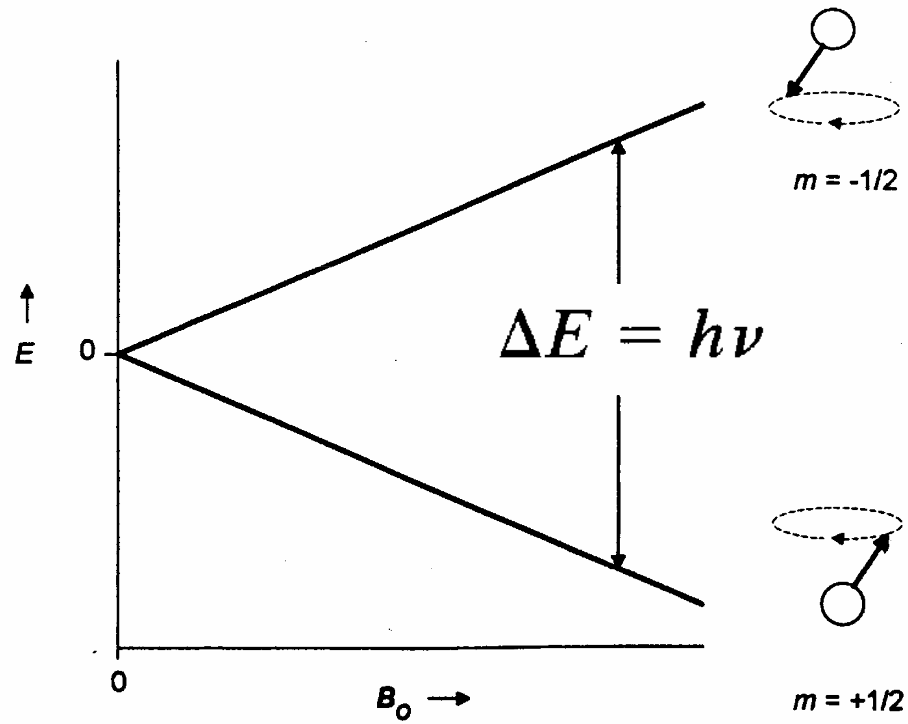
$$\mu = \frac{\gamma I h}{2\pi}$$

when a static magnetic field is applied…

$$E = -\frac{\gamma h}{2\pi} m_I B$$

m_I: magnetic quantum number,
has the values of $-I$, $-I + 1$,.., $I - 1$, I
B: the applied magnetic field

NMR Resonance Condition



Relative energy of both spin states of an $I = \frac{1}{2}$ nucleus as a function of the strength of the external magnetic field $\mathbf{B}_0$.

$$E_i = -m_i \frac{\gamma h \mathbf{B}_0}{2\pi}$$

$\Delta m_I = \pm 1$, therefore…

$$\Delta E = E_{(m=-1/2)} - E_{(m=1/2)}$$

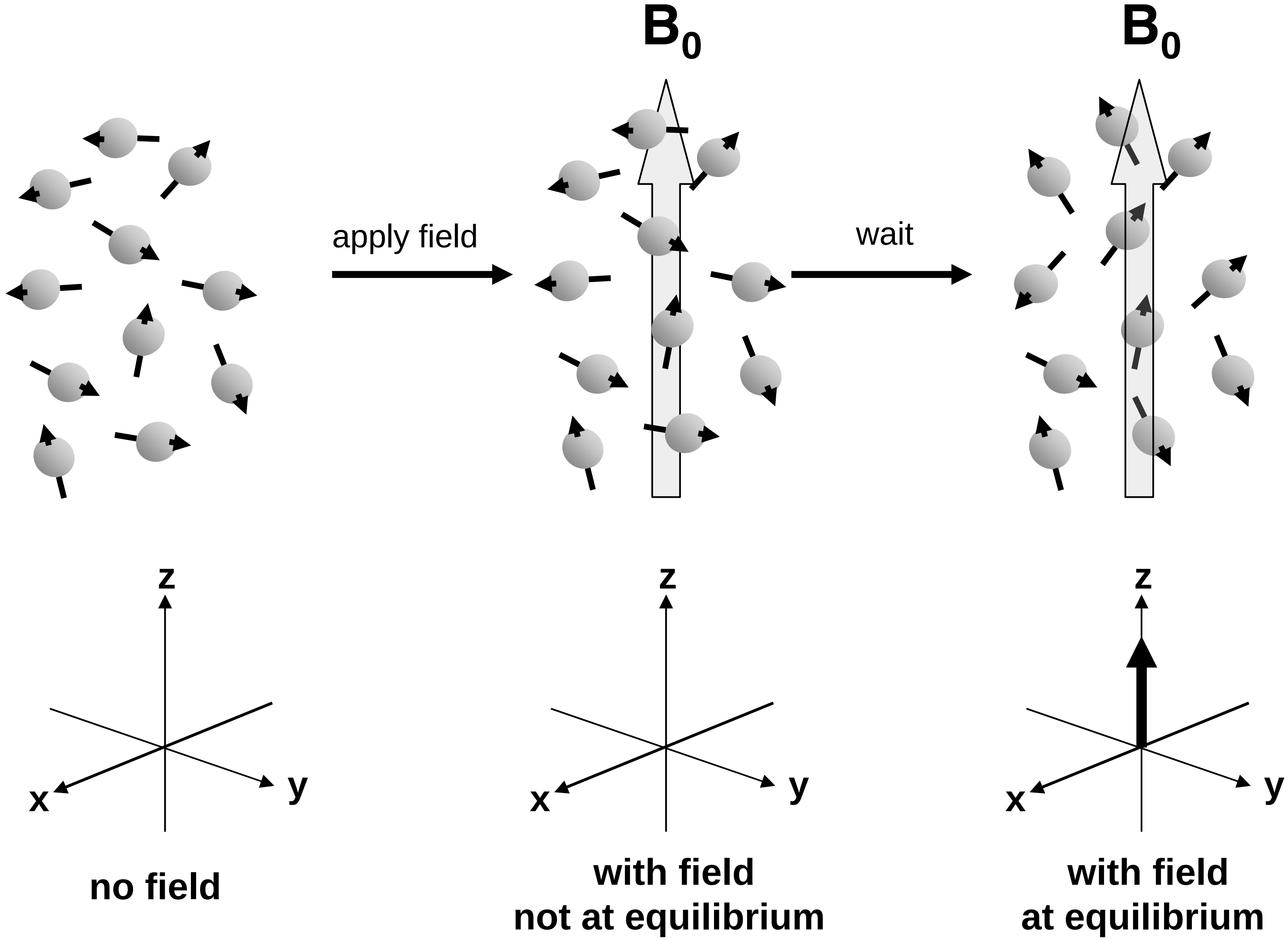
$$\Delta E = \frac{h\gamma}{2\pi} B_0$$

On the other hand…

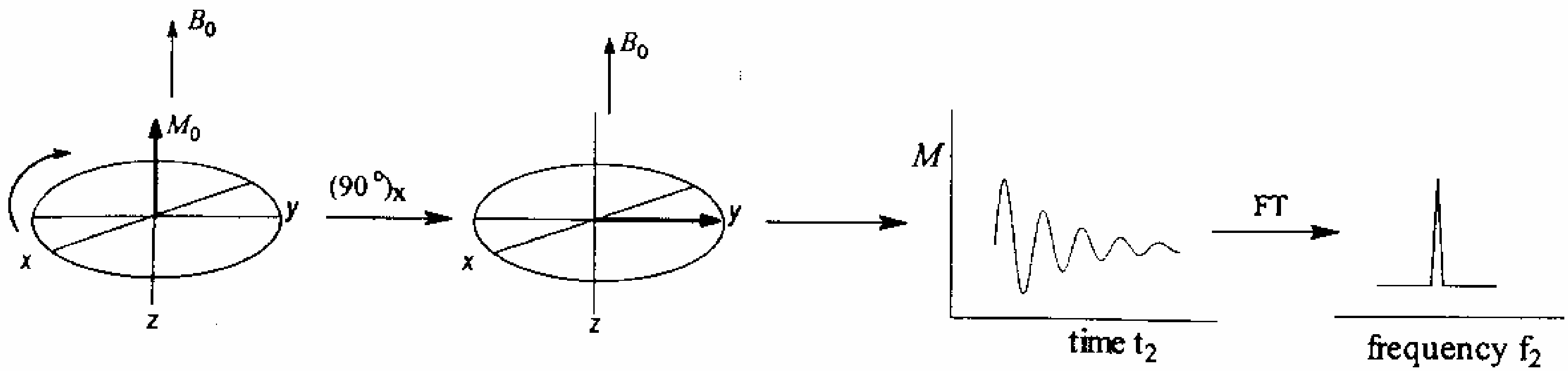
$$\Delta E = h\nu$$

$$\nu = \gamma B_0 / 2\pi$$

Vector Model - A Collection of Spins



Mechanism of Pulsed FT-NMR



Excess of spin population along the direction of applied magnetic field.

After 90° pulse magnetization is tipped into the *xy* plane.

M=Magnetization which produces the FID. It decays as magnetization in *xy* plane diminishes after resonance.

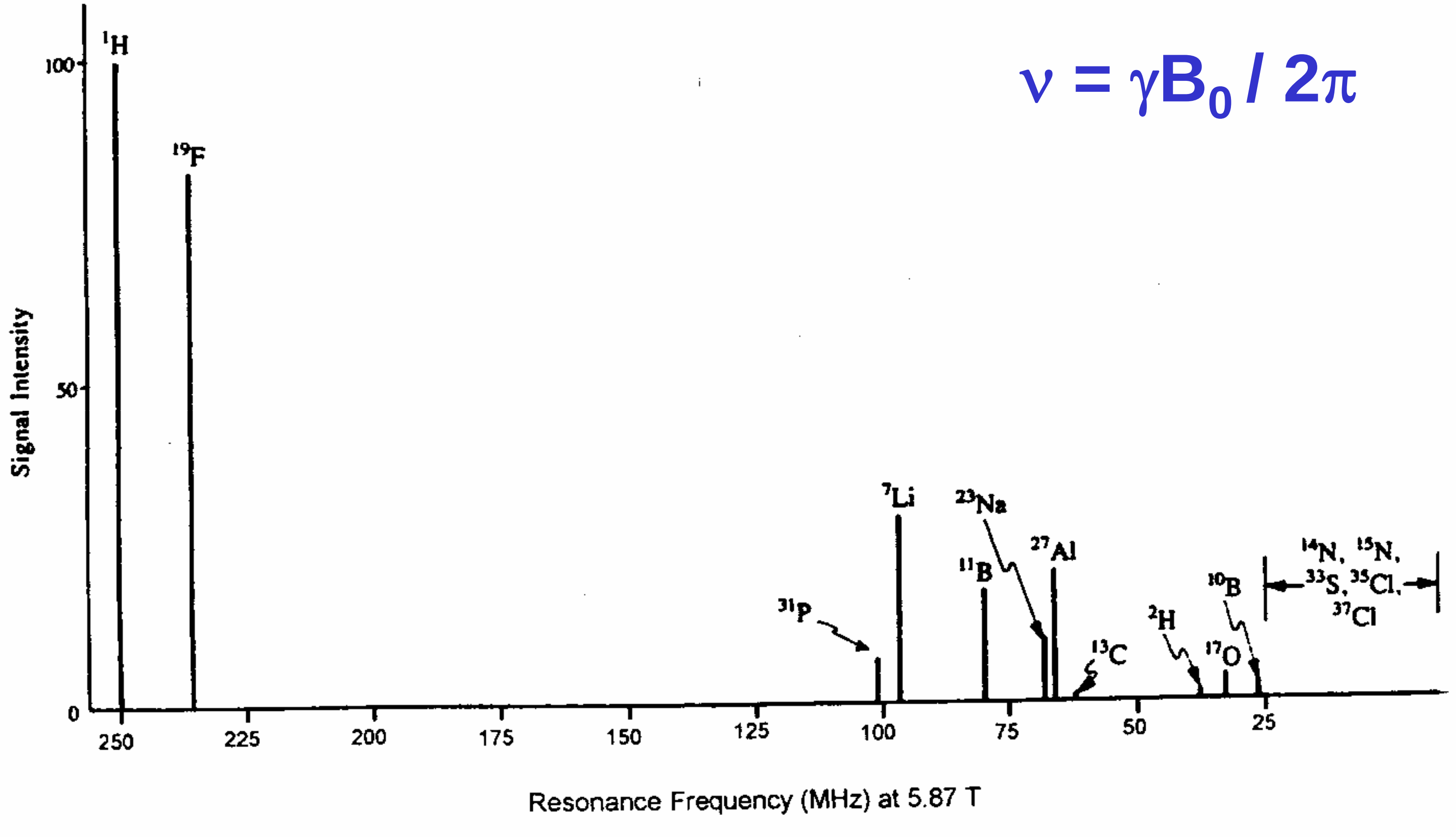
preparation

detection

$$S/N \propto \sqrt{N}$$

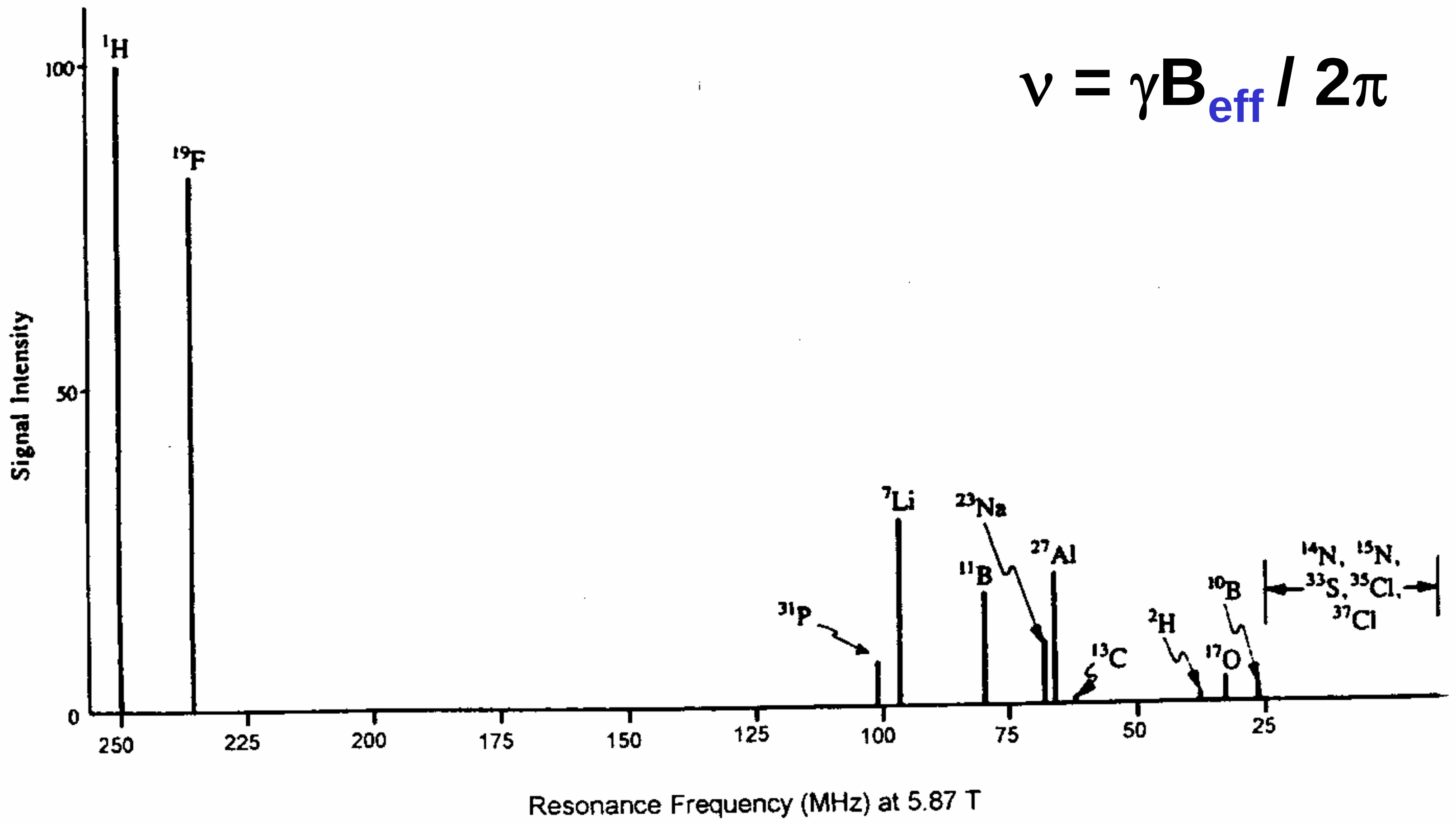
Resonance Frequencies of Common Nucleus (5.87 T)

$$\nu = \gamma B_0 / 2\pi$$



However, life is not that easy…

$$\nu = \gamma B_{eff} / 2\pi$$



Most Important 1D NMR Parameters

^{1}H NMR: Chemical Shift (δ)

Coupling Constant ($J_{H\text{-}H}$)

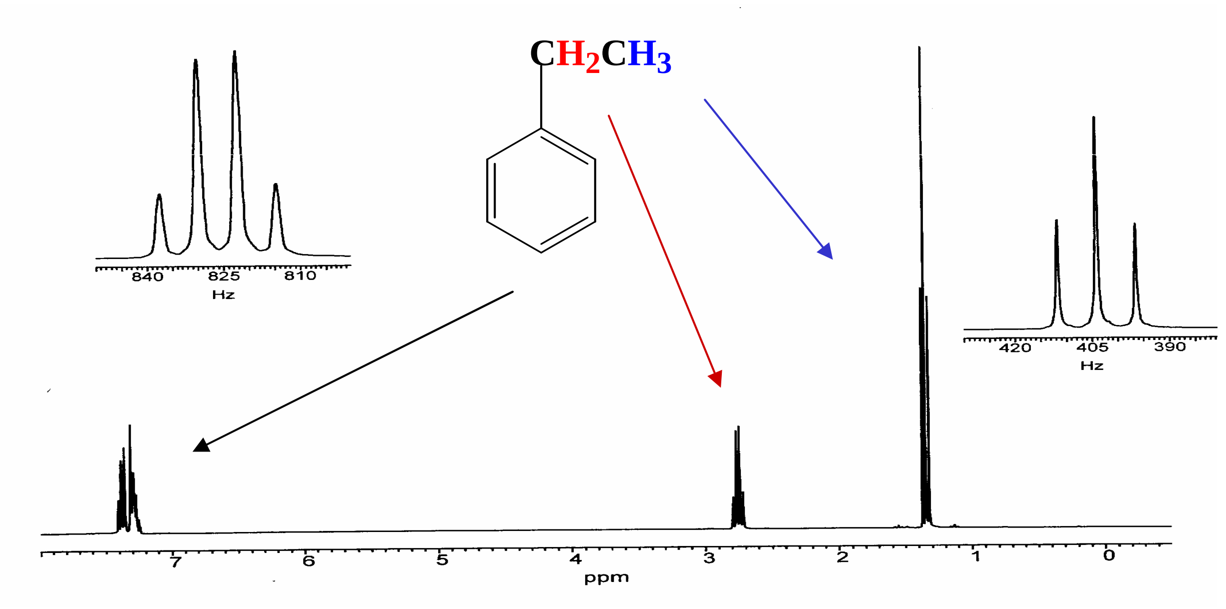
Integration Area (Number of Protons)

^{13}C NMR: Chemical Shift (δ)

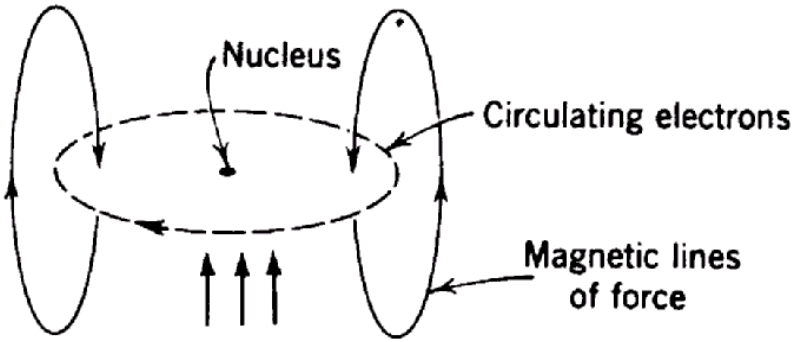
Coupling Constant ($J_{C\text{-}H}$)

Relaxation Time

Chapter 2: Chemical Shift



The Origin of Chemical Shift



$$\nu_1 = \frac{\gamma}{2\pi} B_0$$

$$\nu_{\text{eff}} = \frac{\gamma}{2\pi} B_0(1 - \sigma)$$

$\nu_{eff} < \nu_1$

B_0 = flux density of the stationary magnetic field

ν_1 = applied frequency

ν_{eff} = effective frequency at resonance

γ = magnetogyric ratio

σ = shielding constant

Definition of Chemical Shift (δ)

$$\delta = \frac{\nu_R - \nu_{TMS}}{(\nu_{spectrometer})} \times 10^6$$

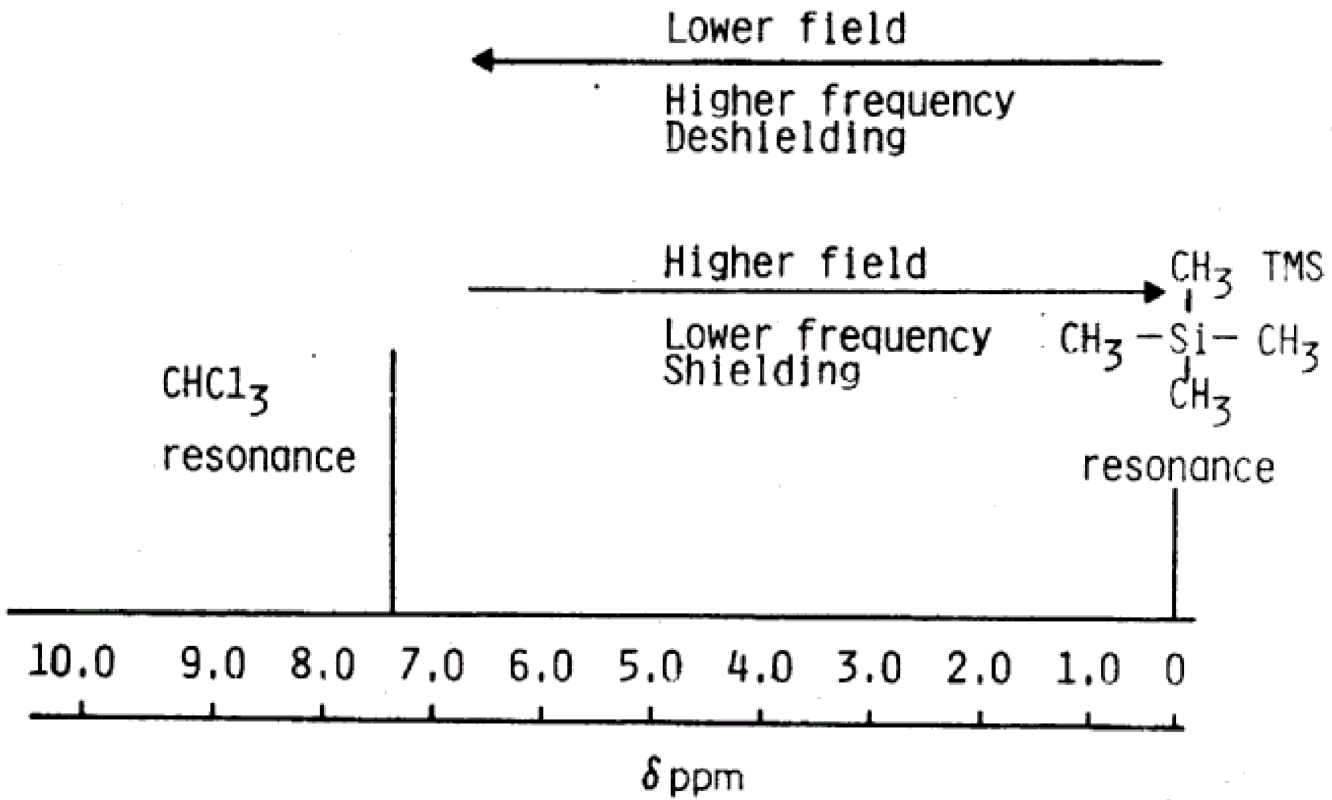
A ratio of frequency difference between the resonance and that of TMS and operating frequency

δ (ppm: part per million)

$$\delta = 3.0 = \frac{\nu_R - \nu_{TMS}}{60 \times 10^6} \times 10^6$$

$$\nu_R - \nu_{TMS} = 60 \times 3.0 = 180 \text{ Hz}$$

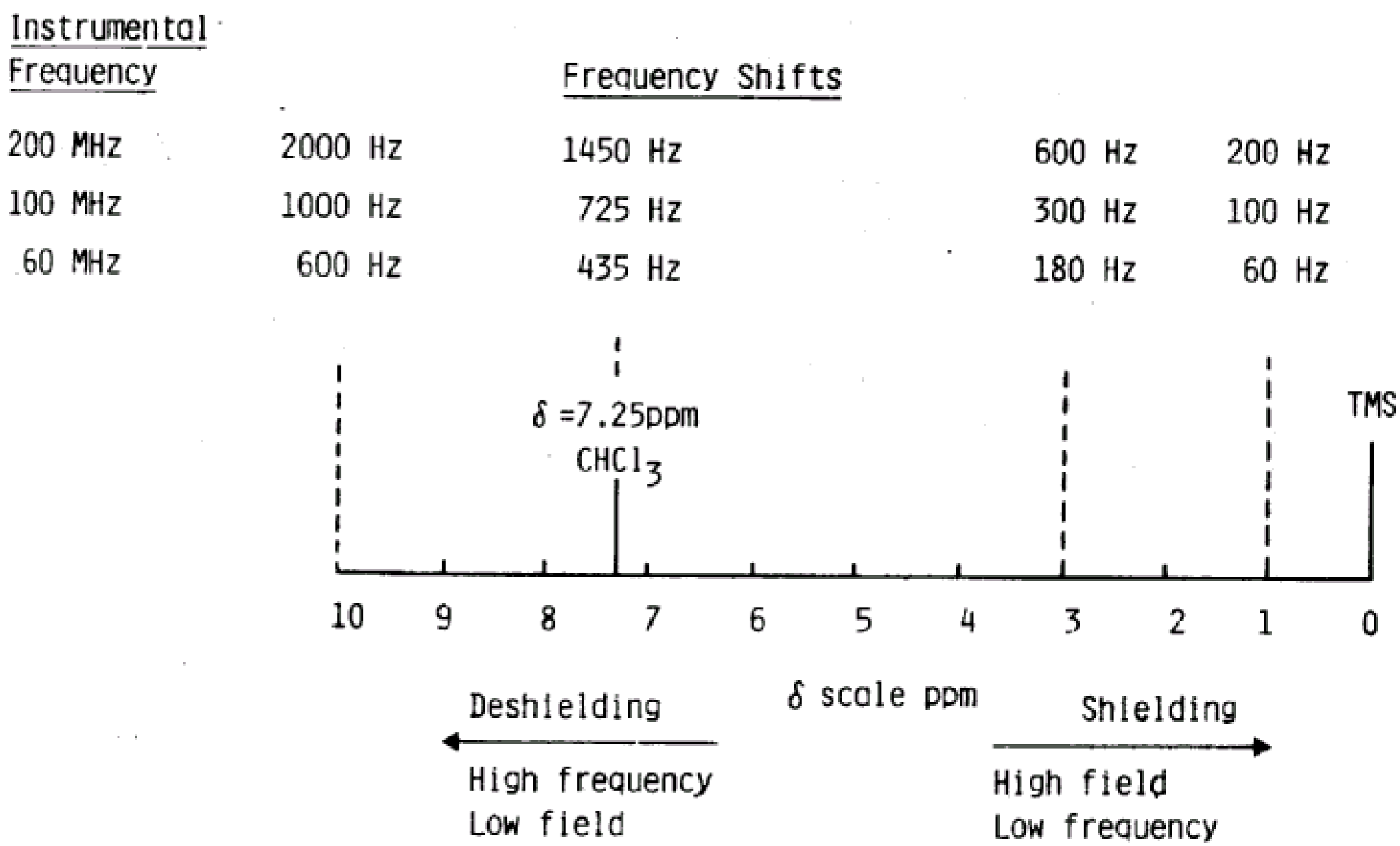
The Relationship between Chemical Shifts, Frequency, Magnetic Field and Shielding in NMR



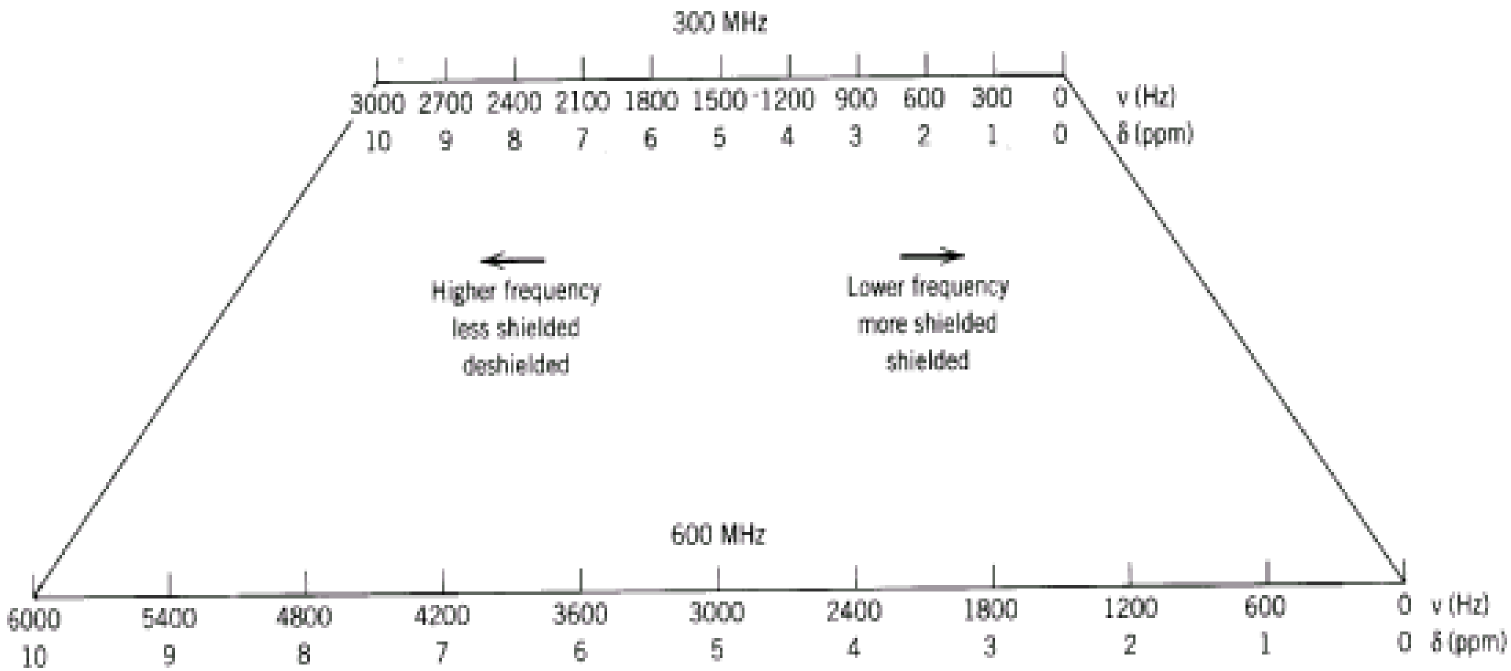
TMS **Tetramethylslane**

DSS **2,2-dimethyl-2-silapentane-5-sulfonate**

Relationship between Radio Frequency and Chemical Shift



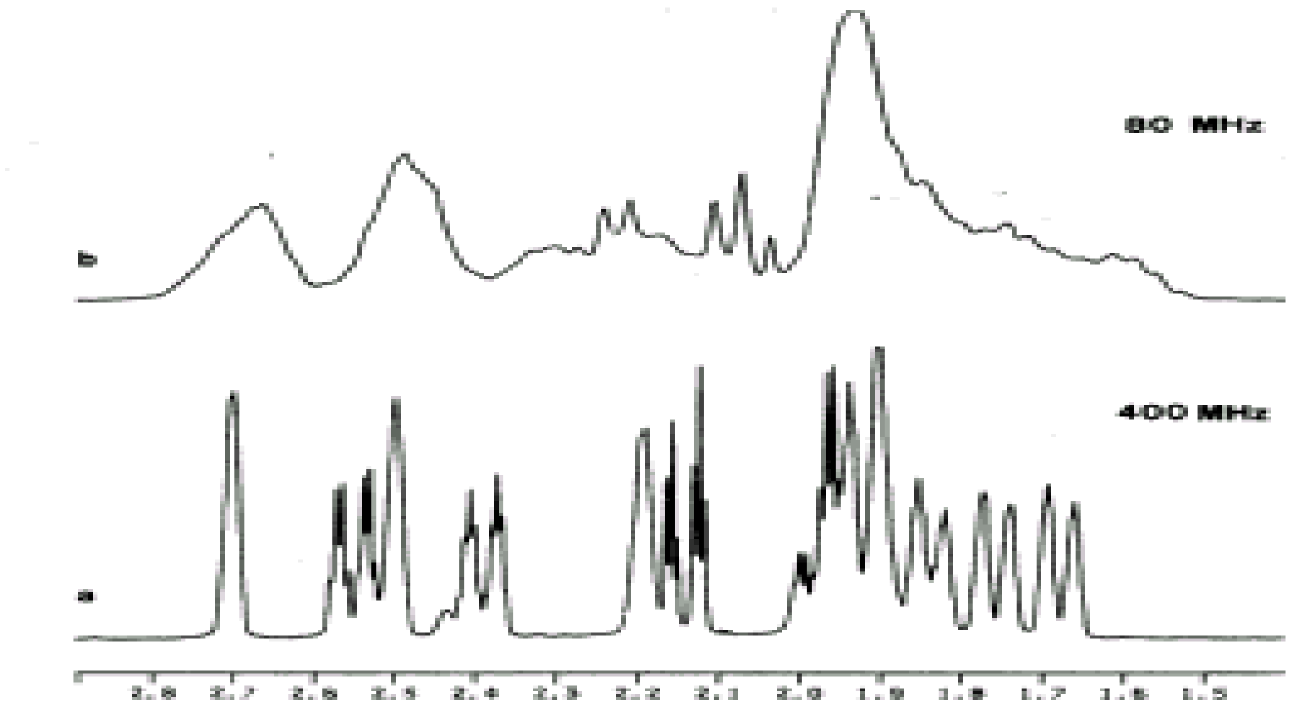
NMR Scale at 300 MHz and 600 MHz Frequency Scan or Pulse



$$\frac{300}{300 \times 10^6} \times 10^6 = \delta\, 1.00, \text{ or } 1.00 \text{ ppm}$$

$$\frac{600}{600 \times 10^6} \times 10^6 = \delta\, 1.00, \text{ or } 1.00 \text{ ppm}$$

Resolution *v.s.* Instrument Frequency



Theory of Chemical Shift

$B_1 = - \sigma B_0$

B Magnetic Field Strength

σ Shielding Constant

In Molecules: $\sigma = \sigma_d + \sigma_p$

In Bigger Molecules: $\sigma = \sigma_d(\mathrm{loc}) + \sigma_p(\mathrm{loc}) + \sigma_a + \sigma_r + \sigma_e + \sigma_s$

σ_d Diamagnetic Shielding Effect

σ_p Paramagnetic Deshielding Effect

σ_a Anisotropic Shielding Effect

σ_r Ring Current Effect

σ_e Electronic Field Effect

σ_s Solvent Effect

Factors Affecting Chemical Shifts

- **Substitution and Hybridization**
- **Inductive and Conjugative Effects**
- **Anisotropic Effects**
- **van der Waals Force**
- **Hydrogen-Bonding**
- **Solvent Effects**

Substitution and Hybridization

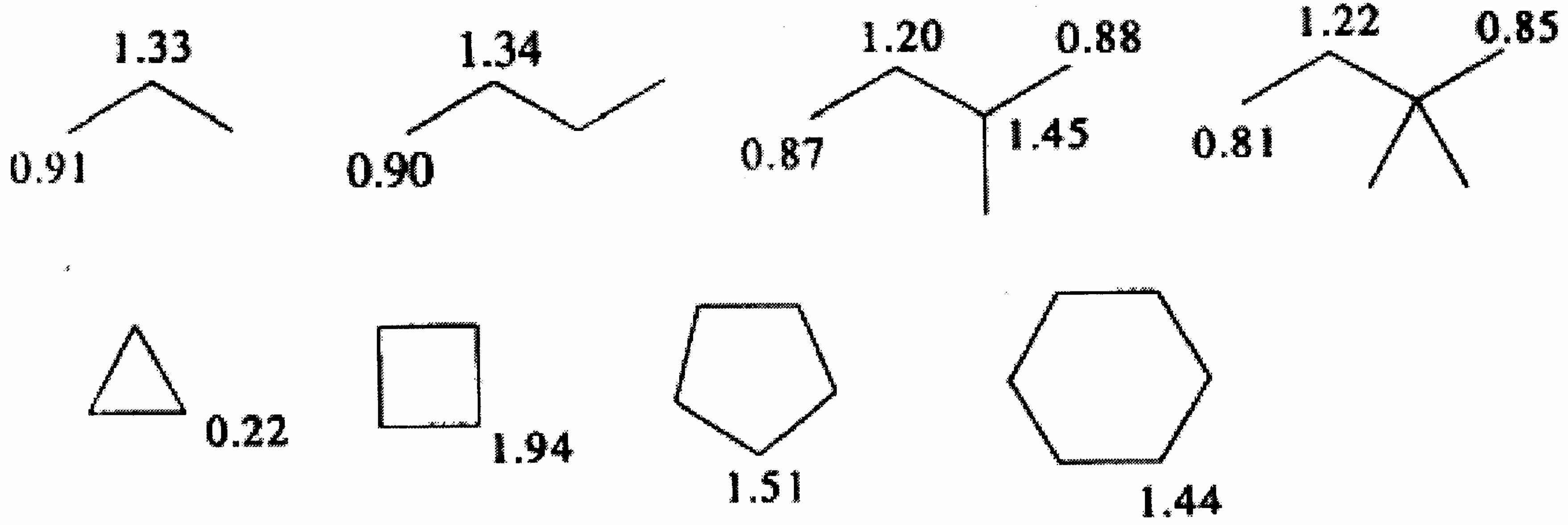
Substitution of a proton by carbon causes deshieiding:

	$R\text{-}CH_3$	$R\text{-}CH_2\text{-}R$	$(R)_2\text{-}CH\text{-}R$	R= alkyl
δ:	0.93	1.2	1.5	

sp^3,sp^2 or sp hybridization of carbon-13 influences the resonance position:

	δ_H (ppm)	δ_C (ppm)
Alkyl (sp^3)	1-4	10-50
Alkenic (sp^2)	5-7	100-150
Aromatic (sp^2)	7-9	100-150
Carbonyl (sp^2)	8-10	150-200
Alkynic (sp)	3	50-80

Examples



Inductive Effect :
Electron Withdrawing Groups Lead to Deshielding

	CH_3-F	CH_3-Cl	CH_3-Br	CH_3-I	CH_3-Si $(CH_3)_3$	CH_3-M
δ:	4.3	3.0	2.7	2.2	0.00	- δ

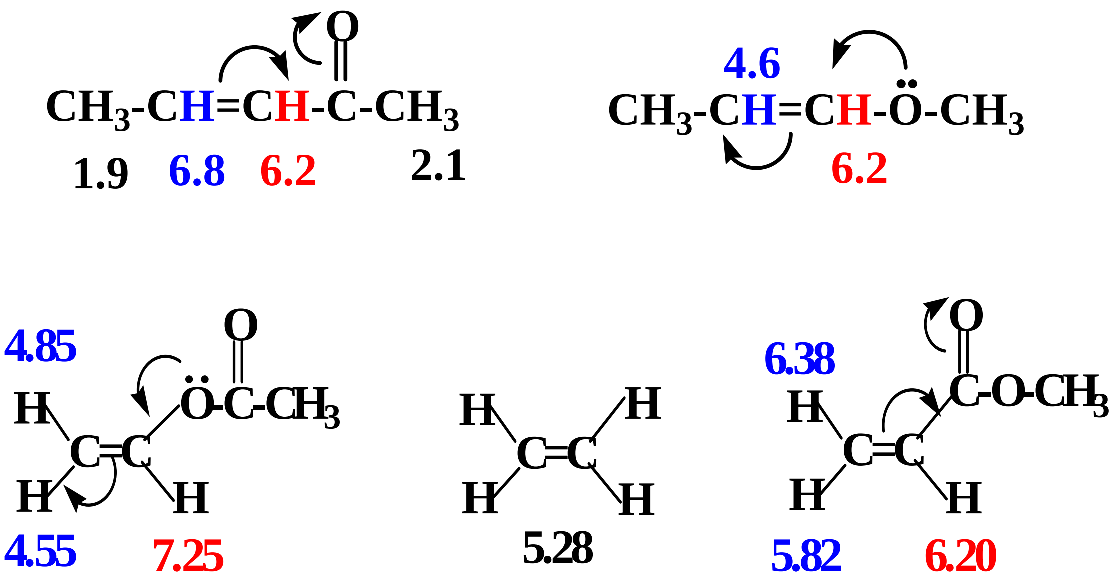
	CH_3-F	CH_3-OH	CH_3-NH_2	CH_3-CH_3
δ:	4.3	3.4	2.2	0.9

	CH_3-Br	CH_3CH_2-Br	CH_3 CH_2 CH_2-Br	CH_3 CH_2 CH_2 CH_2 CH_2 CH_2-Br
δ:	2.7	1.7	1.0	0.90

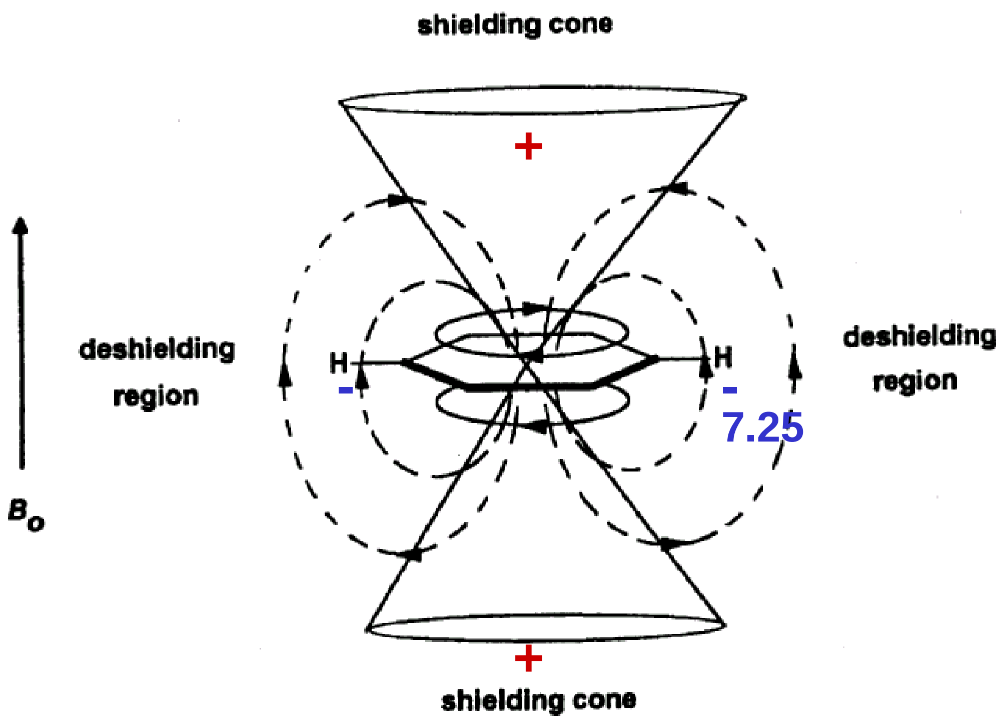
	F-CH_2-F	Cl-CH_2-Cl	Br-CH_2-Br	I-CH_2-I
δ:	5.5	5.3	4.9	3.9

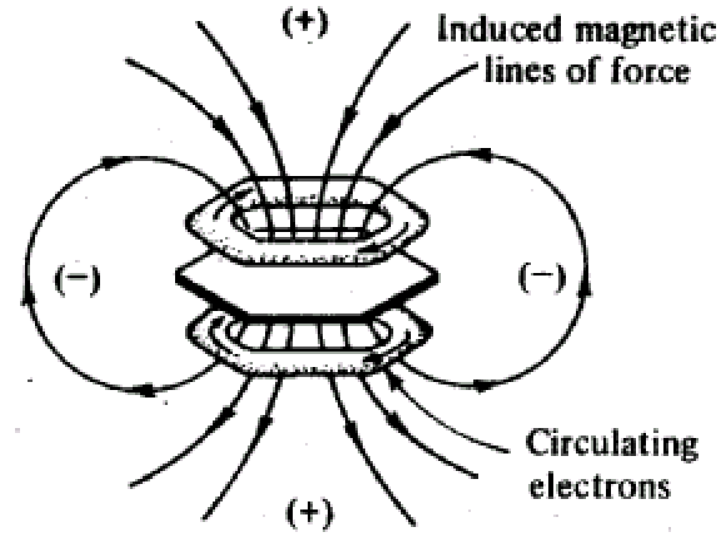
	CH_3Cl	CH_2Cl_2	$CHCl_3$
δ:	3.0	3.3	7.27

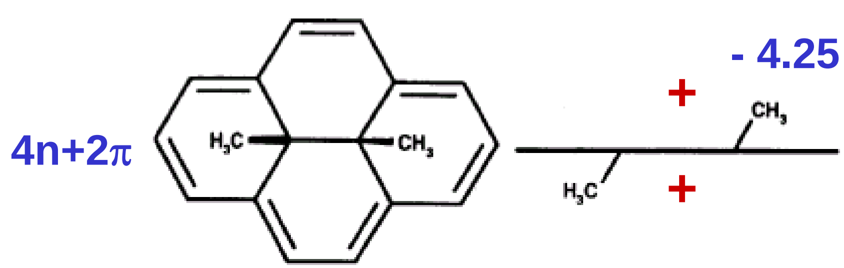
Conjugative Effect : Shielding



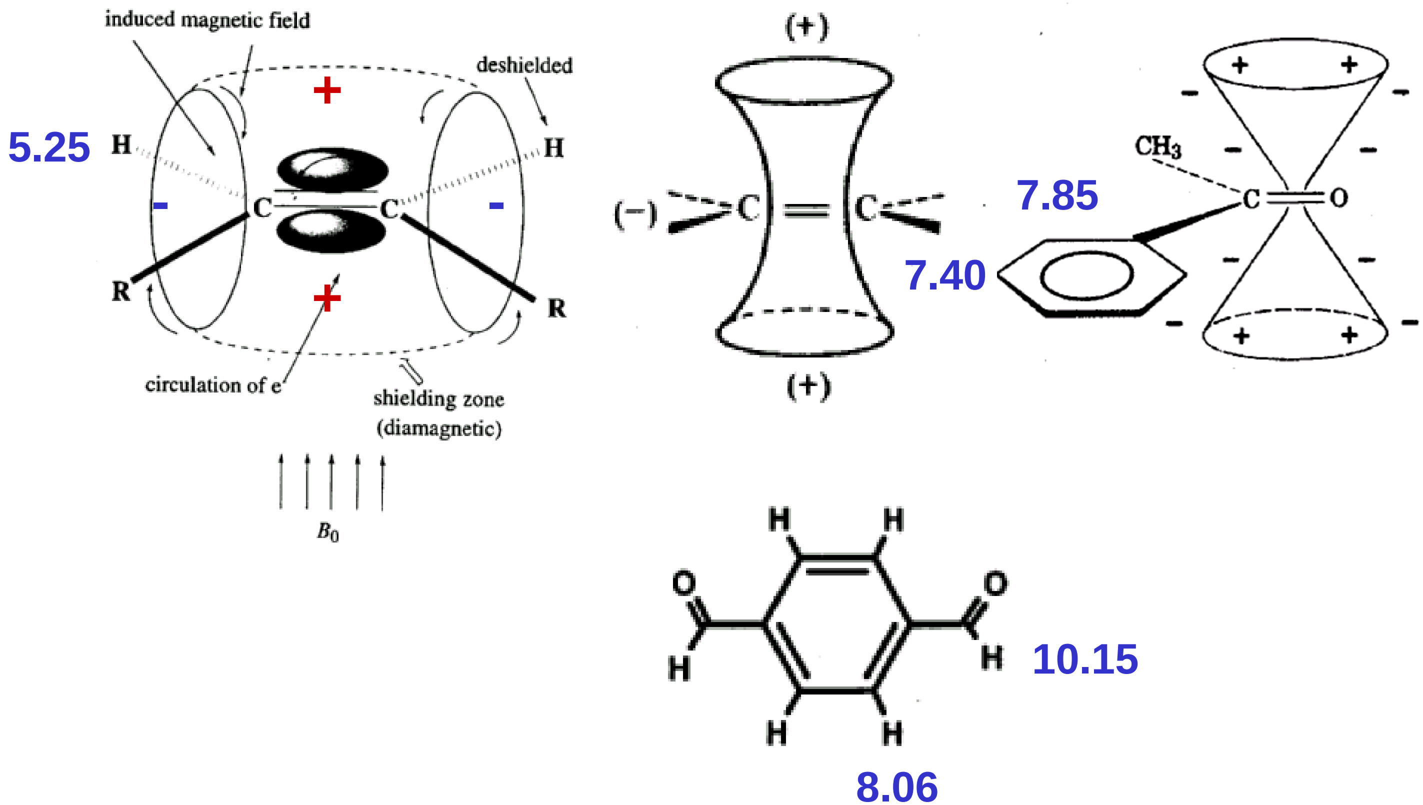
Anisotropic Effect of Aromatic Rings





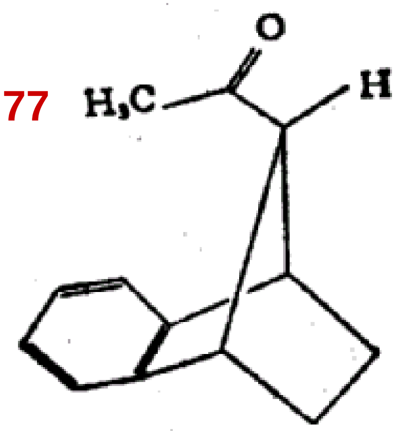


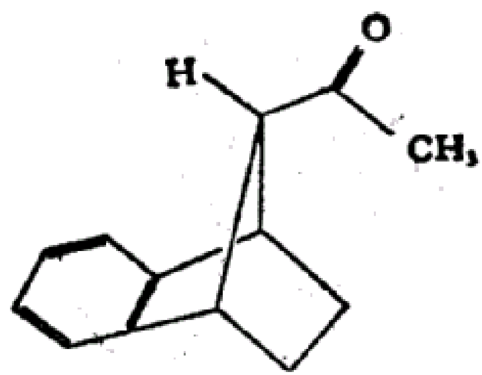
Anisotropic Effect of Double Bonds



Examples

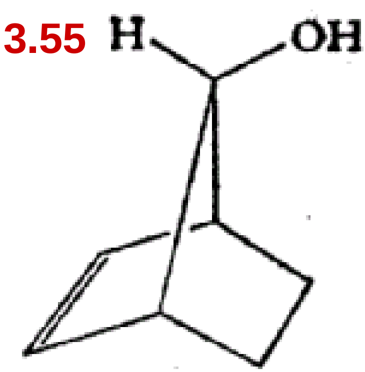
1.77

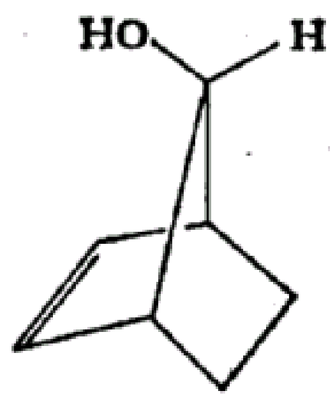




2.31

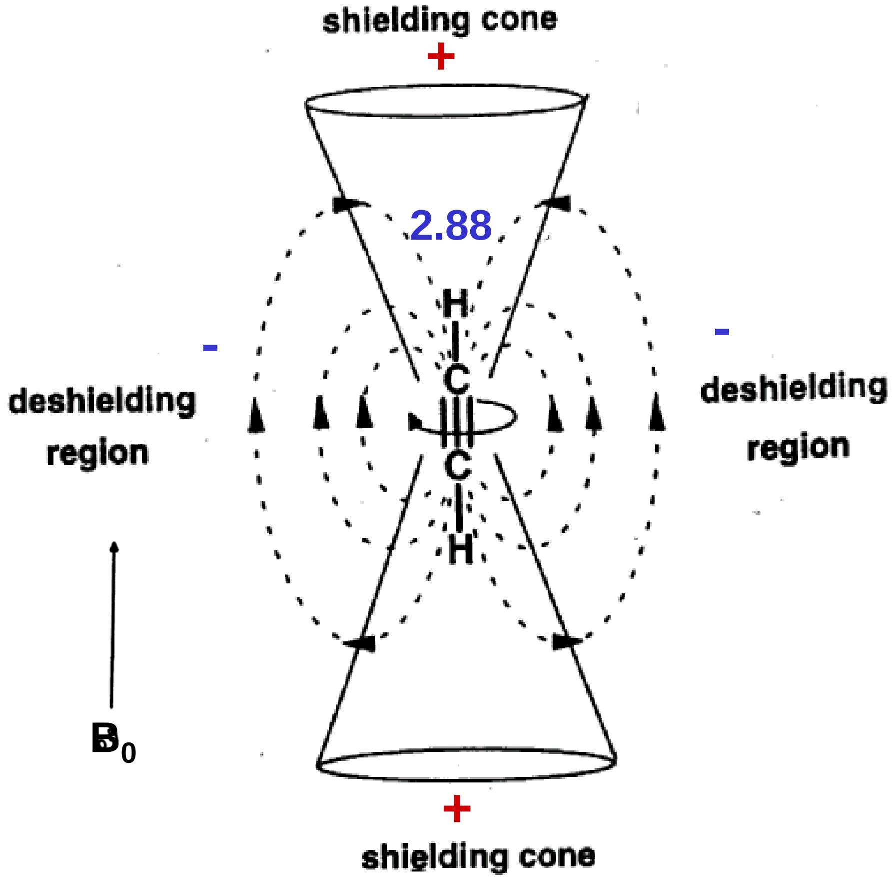
3.55

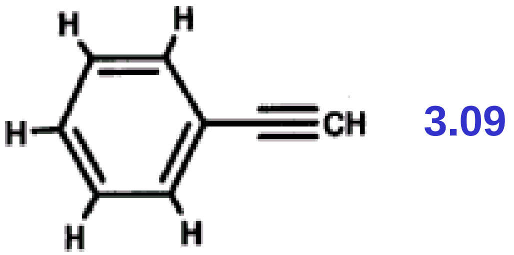




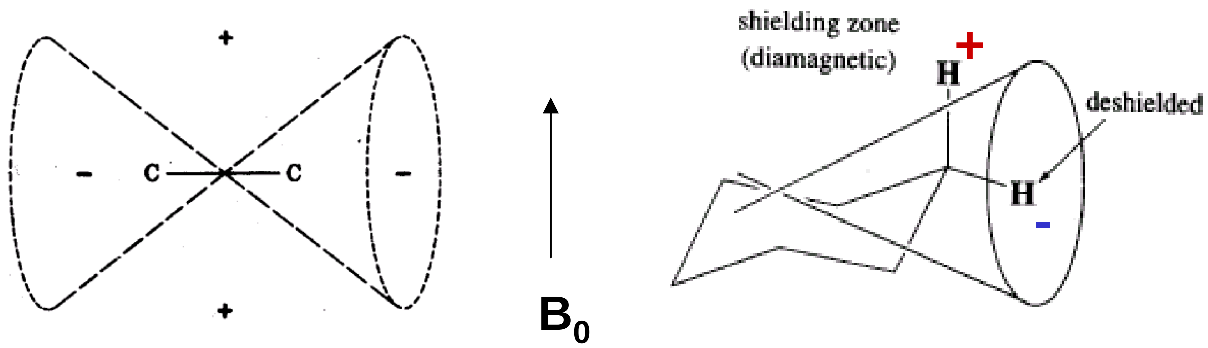
3.75

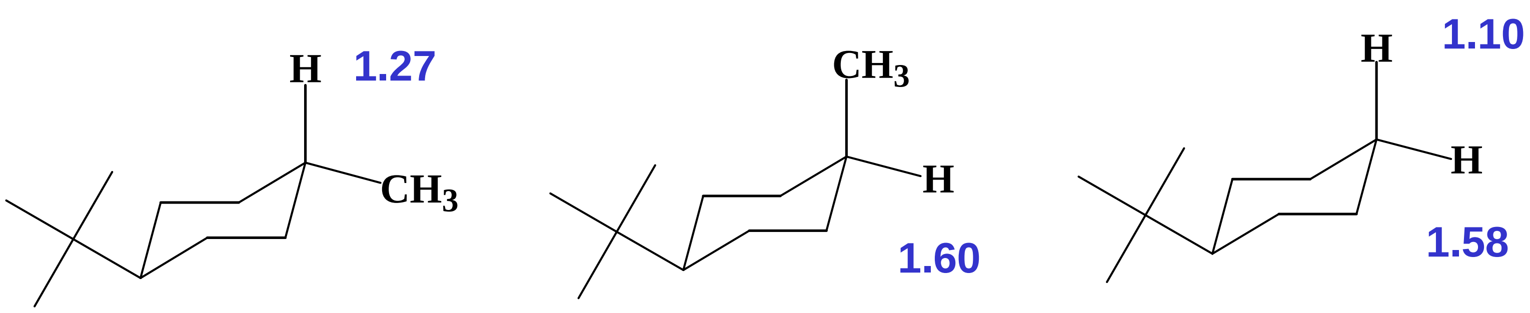
Anisotropic Effect of Triple Bond



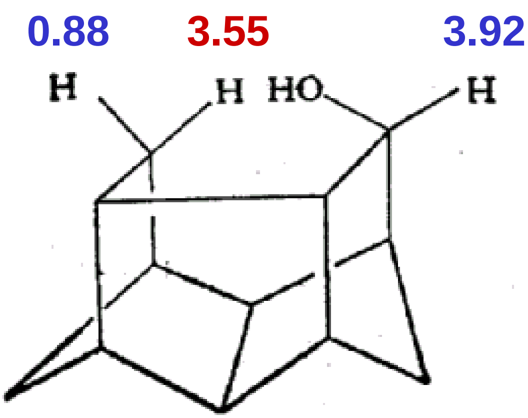


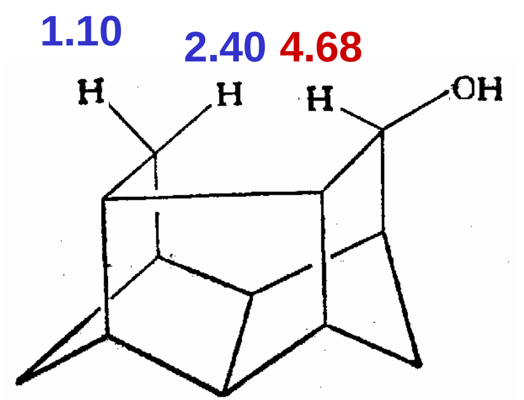
Anisotropic Effect of Single Bond

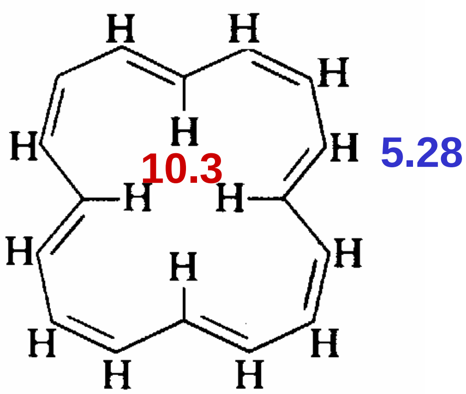




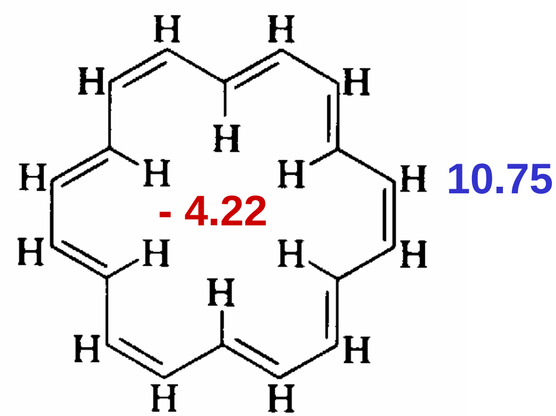
van der Waals Force







[16]-annulene



[18]-annulene

Hydrogen-Bonding

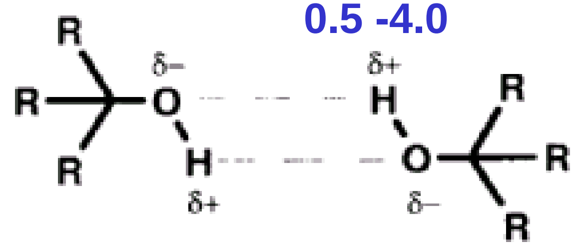
Intermolecular hydrogen-bonding

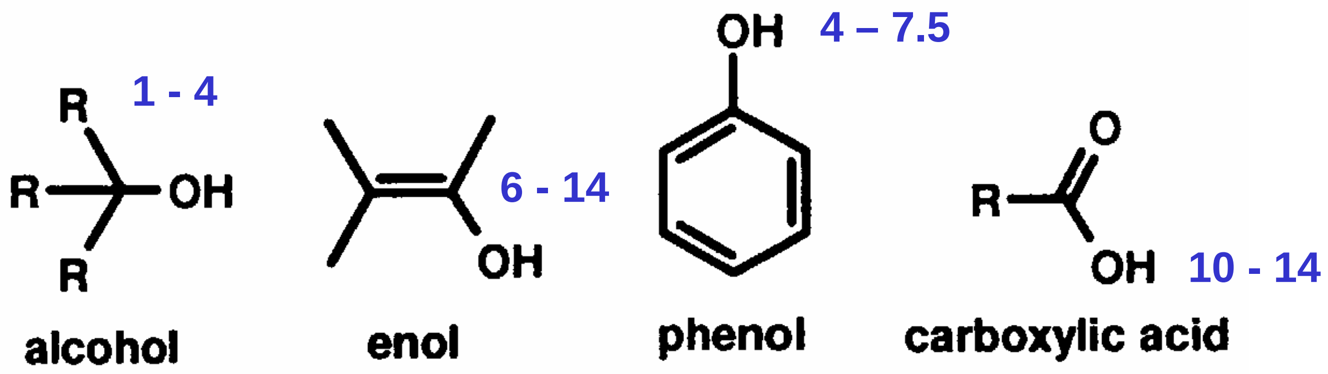
(δ influenced by solvents)

X-H----Y

X = N,O,Cl,Br,…

0.5 -4.0



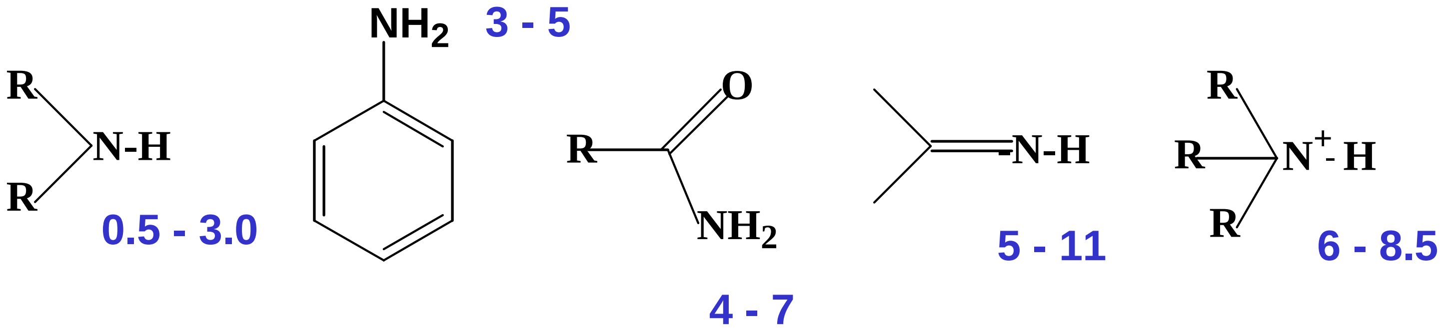


δ depends on temperature, concentration and the nature of the solvent.

Hydrogen-Bonding

Intermolecular hydrogen-bonding

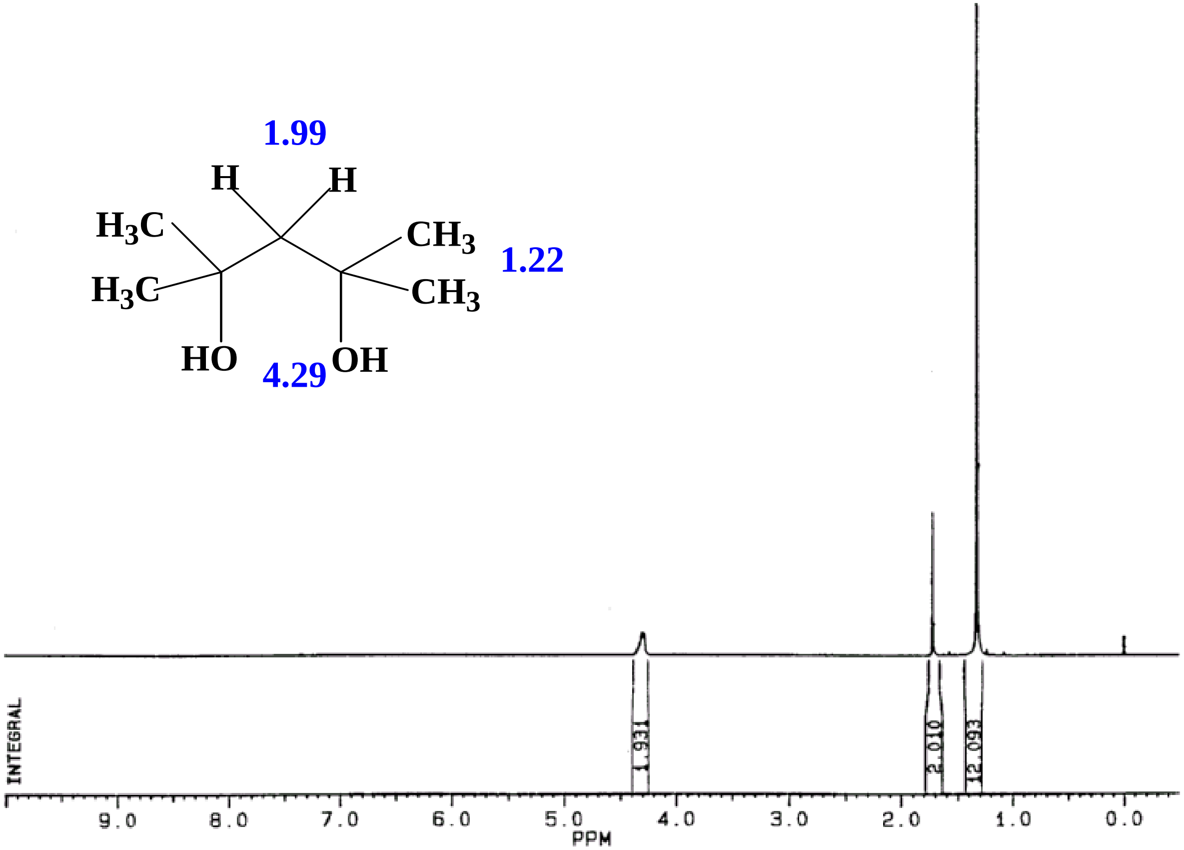
(δ influenced by solvents)



Intra-molecular Hydrogen-Bonding

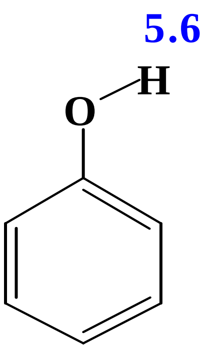
$(R)_3 - OH$

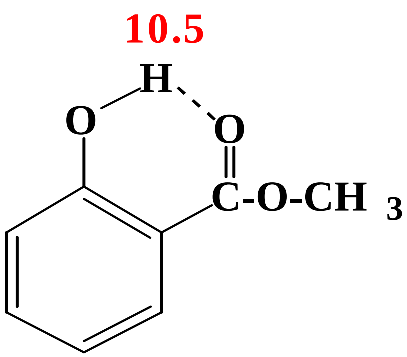
δ **1- 4**

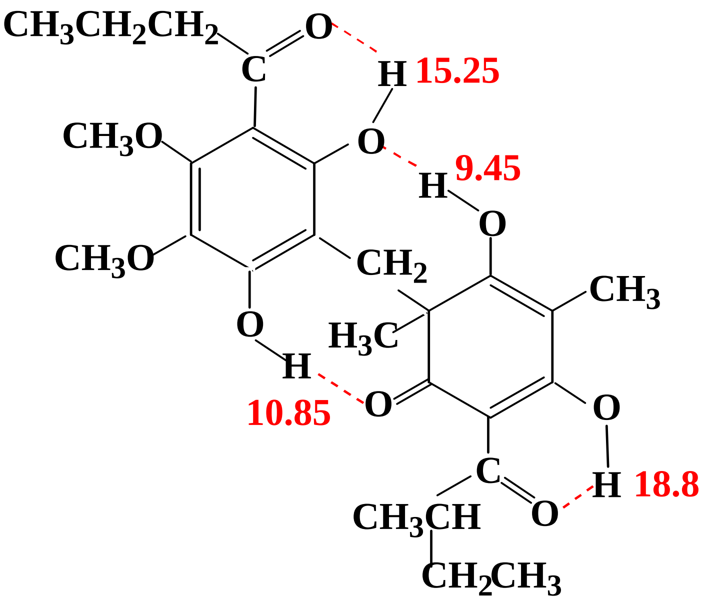


Hydrogen-Bonding

Intramolecular hydrogen-bonding
(δ not influenced by solvents)

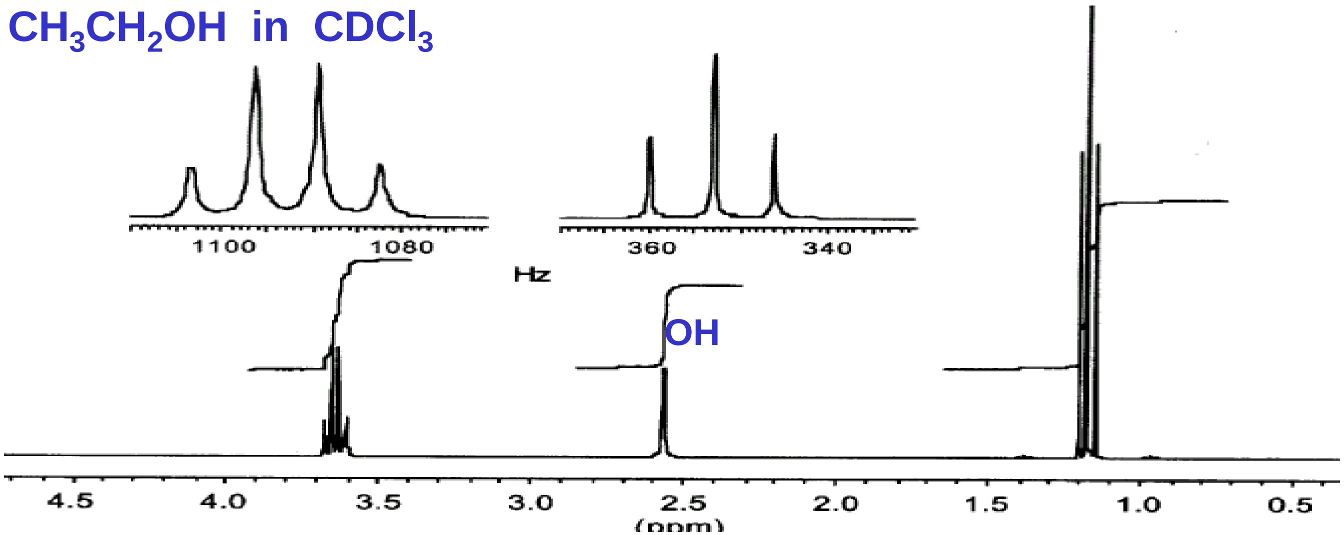




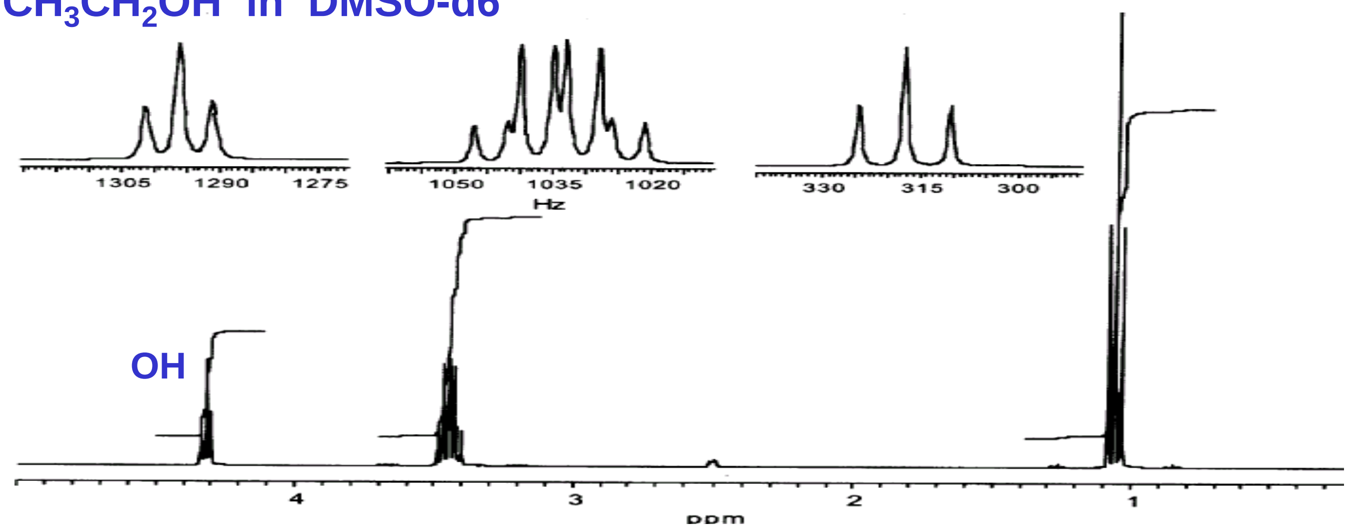


Solvents Effects

CH_3CH_2OH in $CDCl_3$



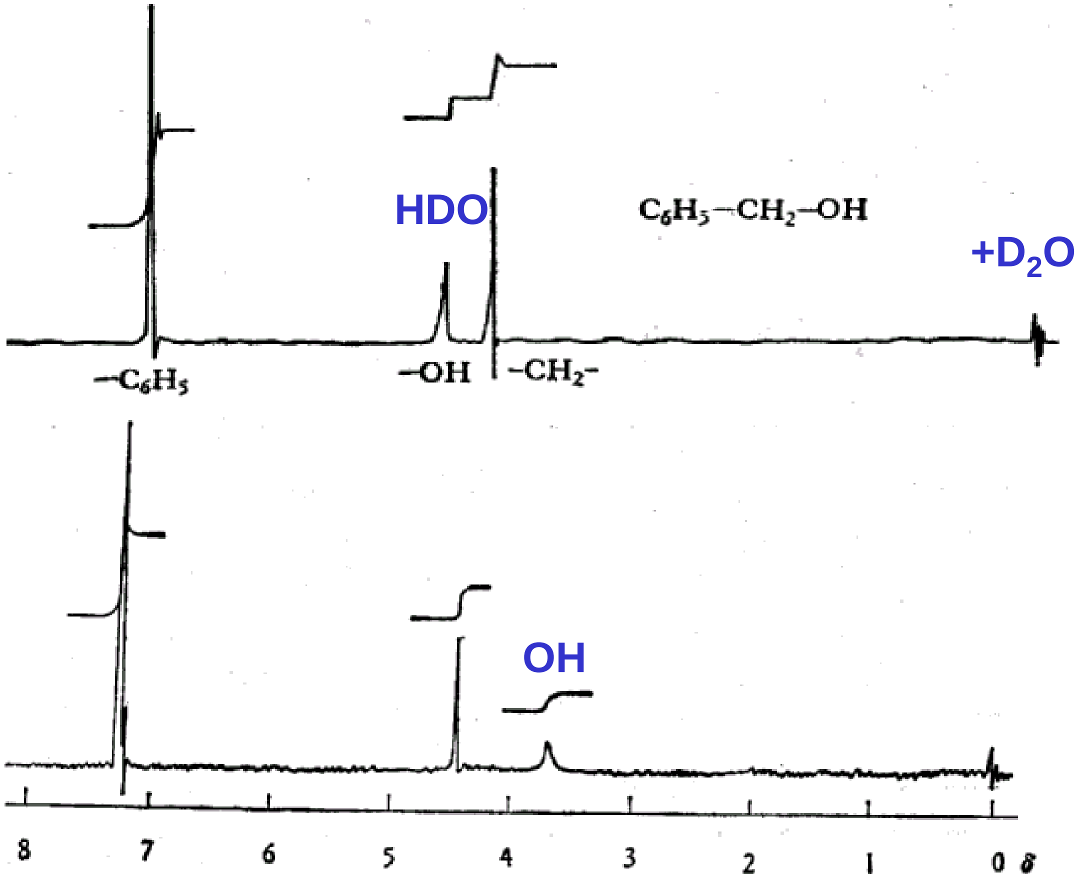
CH_3CH_2OH in DMSO-d6



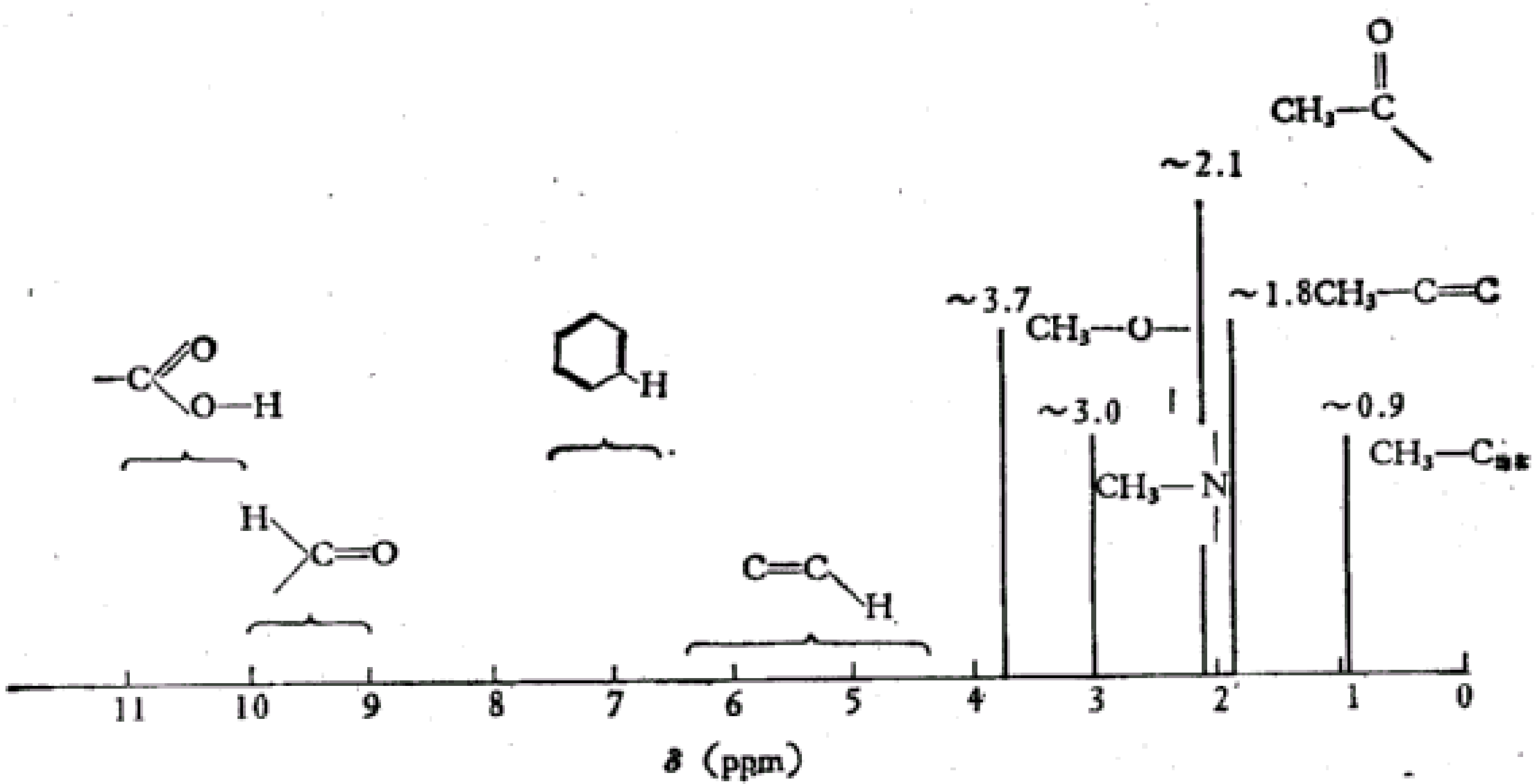
Solvents Effects

D_2O Exchange for determining active hydrogens in R**OH**, RCO**OH** and R_2**NH**, RCO**NH$_2$**

$$ROH + D_2O \longrightarrow ROD + HDO$$



^{1}H Chemical Shifts of Common Structures



Some Useful NMR Solvents

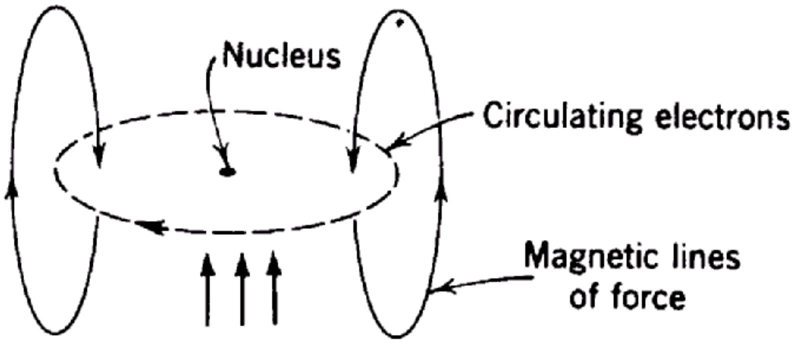
Solvent	δ_H ppm	δ_C ppm	δHDO ppm
Acetone-d_6	2.05 (5)	206.7 (13)	2.0
		29.9 (7)	
Acetonitrile-d_3	1.94 (5)	118.7 (1)	2.1
		1.4 (7)	
Benzene-d_6	7.16 (1)	128.4 (3)	0.4
Choloform-d	7.27 (1)	77.2 (3)	4.8
Cyclohexane-d_{12}	1.38 (1)	26.4 (5)	
D_2O	4.8		4.8
p-Dioxane-d_6	3.53 (m)	66.7 (5)	2.4
DMSO-d6	2.50 (5)	39.5 (7)	3.3
Methanol-d_4	3.31 (5)	49.2 (7)	5.0
	4.87 (1)		
Pyridine-d_5	7.22 (1)	123.9 (3)	5.0
	7.58 (1)	135.9 (3)	
	8.74 (1)	150.4 (3)	

In last course, we were talking about…

In last course, we were talking about…

- Origin of Chemical Shift
- Definition of Chemical Shift
- Theory of Chemical Shift
- Factors Affecting Chemical Shift
- ^{1}H Chemical Shifts of Common Structures

The Origin of Chemical Shift



B_0

$\nu_{eff} < \nu_1$

$$\nu_1 = \frac{\gamma}{2\pi} B_0$$

$$\nu_{eff} = \frac{\gamma}{2\pi} B_0(1 - \sigma)$$

B_0 = flux density of the stationary magnetic field

ν_1 = applied frequency

ν_{eff} = effective frequency at resonance

γ = magnetogyric ratio

σ = shielding constant

Definition of Chemical Shift (δ)

$$\delta = \frac{\nu_R - \nu_{TMS} \times 10^6}{(\nu_{spectrometer})}$$

A ratio of frequency difference between the resonance and that of TMS and operating frequency

δ (ppm: part per million)

$$\delta = 3.0 = \frac{\nu_R - \nu_{TMS}}{60 \times 10^6} \times 10^6$$

$$\nu_R - \nu_{TMS} = 60 \times 3.0 = 180 \text{ Hz}$$

Theory of Chemical Shift

$B_1 = -\sigma B_0$

B Magnetic Field Strength

σ Shielding Constant

In Molecules: $\sigma = \sigma_d + \sigma_p$

In Bigger Molecules: $\sigma = \sigma_d(\mathrm{loc}) + \sigma_p(\mathrm{loc}) + \sigma_a + \sigma_r + \sigma_e + \sigma_s$

σ_d Diamagnetic Shielding Effect

σ_p Paramagnetic Deshielding Effect

σ_a Anisotropic Shielding Effect

σ_r Ring Current Effect

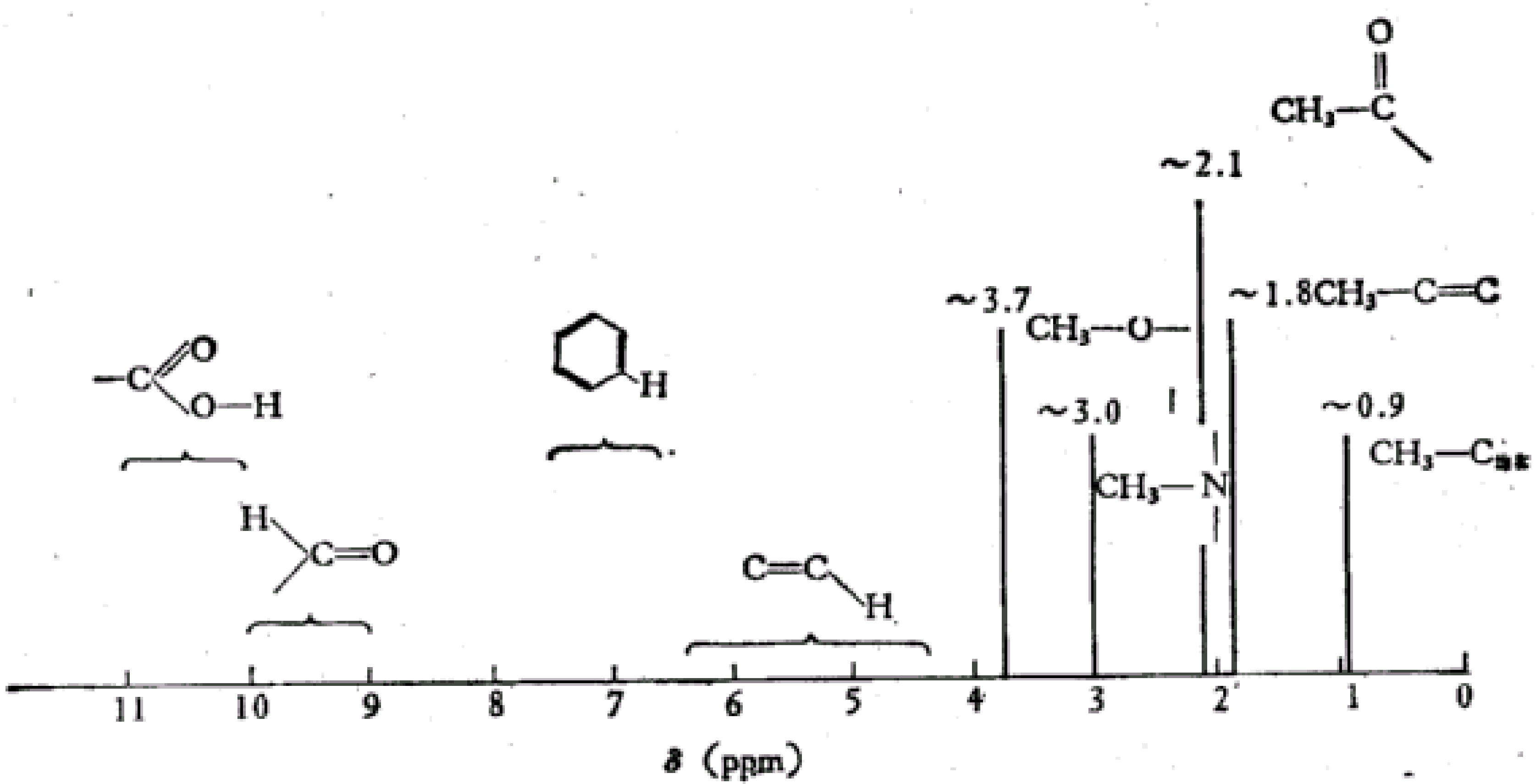
σ_e Electronic Field Effect

σ_s Solvent Effect

Factors Affecting Chemical Shifts

- **Substitution and Hybridization**
- **Inductive and Conjugative Effects**
- **Anisotropic Effects**
- **van der Waals Force**
- **Hydrogen-Bonding**
- **Solvent Effects**

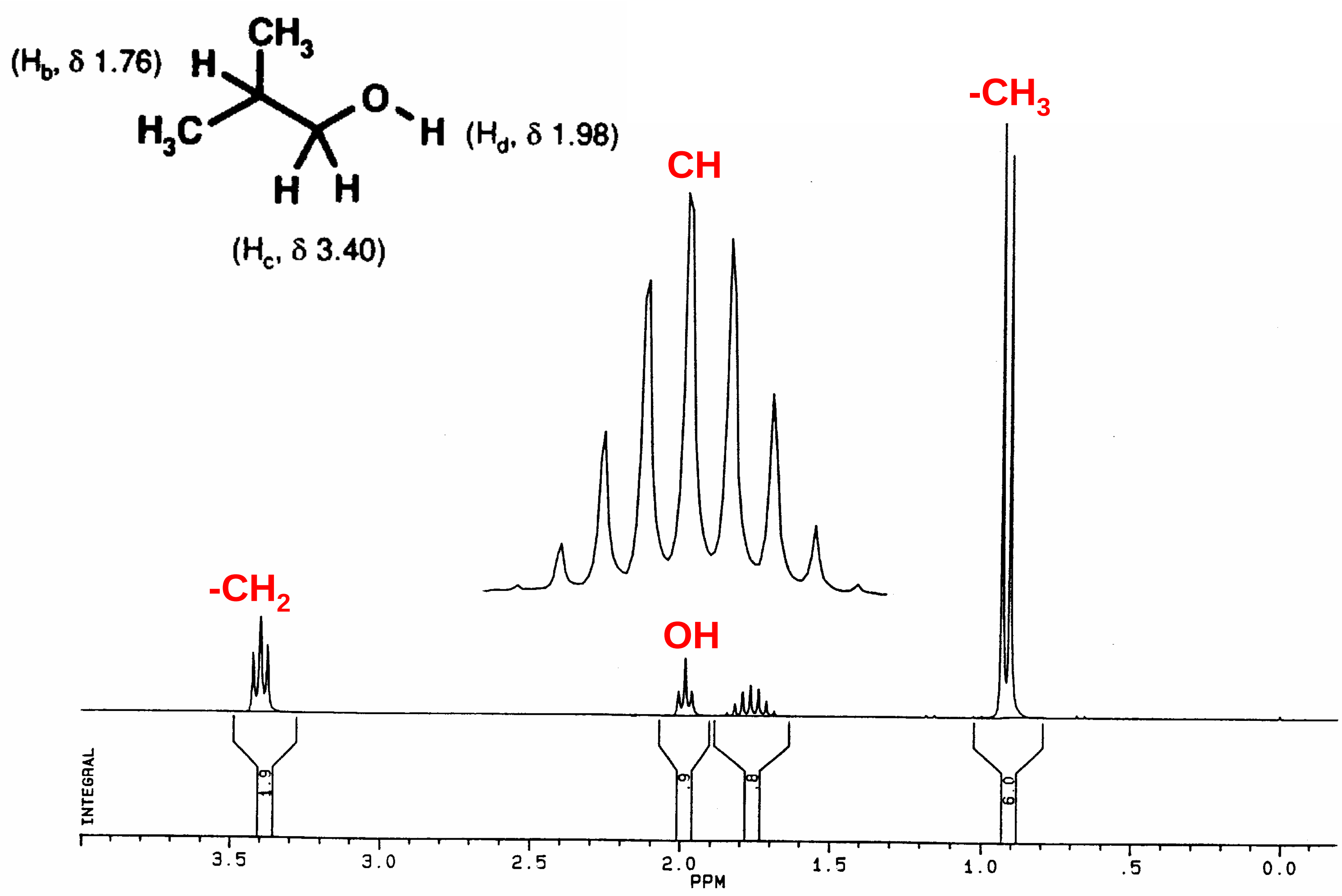
^{1}H Chemical Shifts of Common Structures



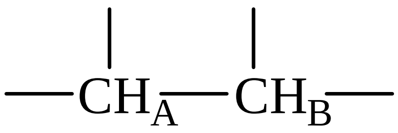
Chapter 3:
Spin-Spin Coupling and Spin Systems

- **Mechanism of Spin-Spin Coupling**
- **Homonuclear ^{1}H Coupling**
- **n + 1 Rule in First-Order Spectra**
- **Heteronuclear Coupling**
- **Chemical Shift Equivalence and Magnetic Equivalence**
- **Multipletes for Various Types of Spin Systems**

Proton Spin-Spin Coupling

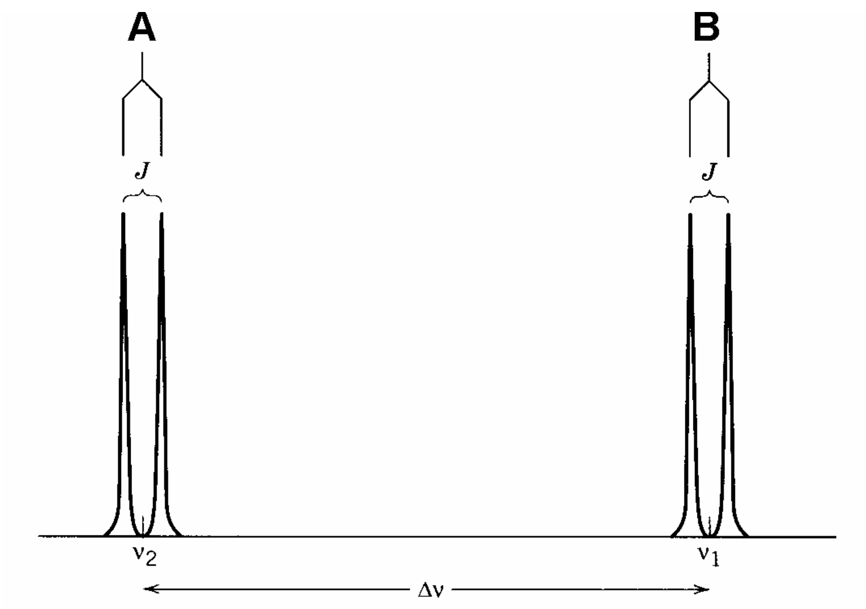


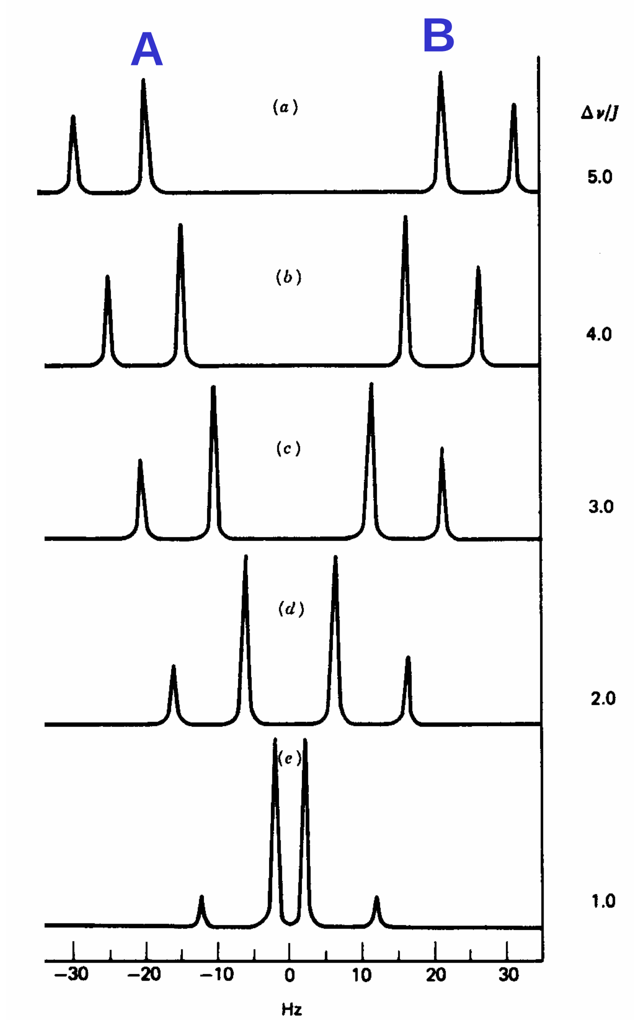
The Mechanism of Spin-Spin Coupling



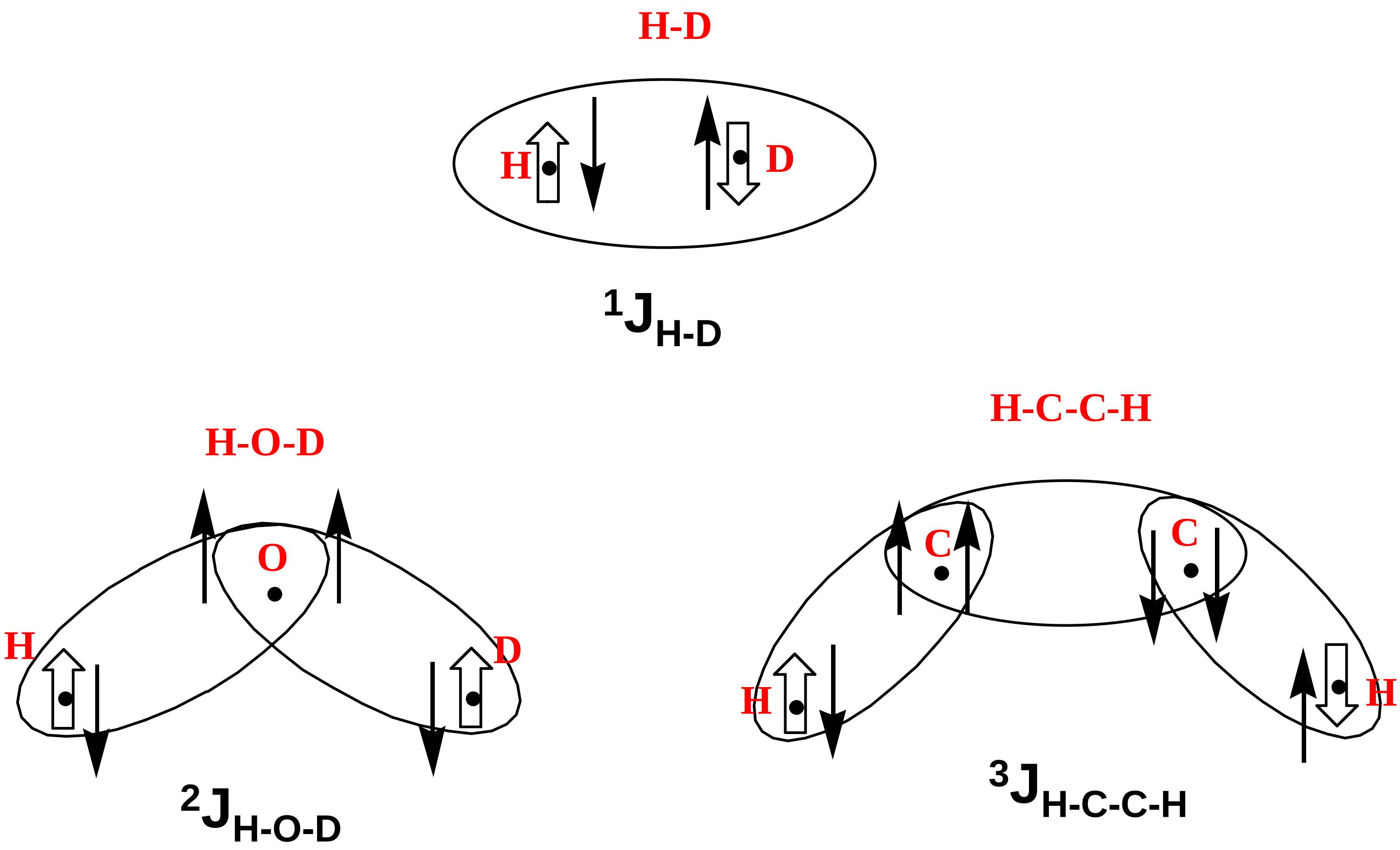
$$H_A = H_0 (1- \sigma_A) \pm H_B'$$

$$H_B = H_0 (1- \sigma_B) \pm H_A'$$





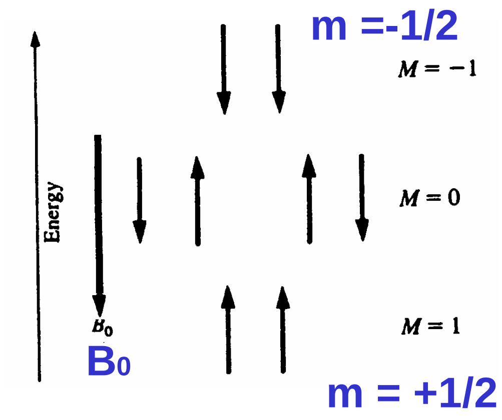
The Mechanism of Spin-Spin Coupling
Dirac Model of J Coupling



Homonuclear ^{1}H Coupling: The Simplified Picture

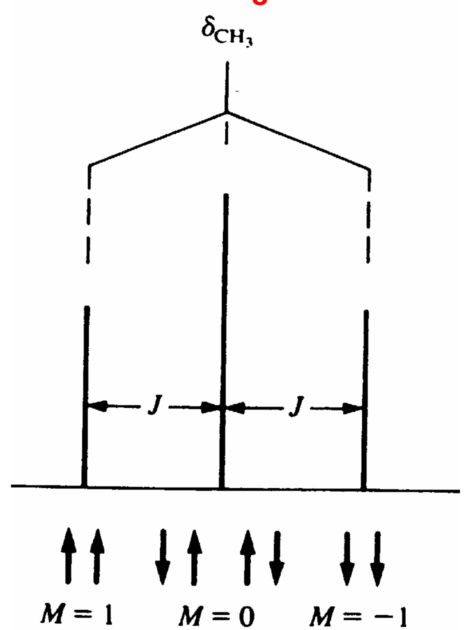
$-CH_2-CH_3$

CH_2



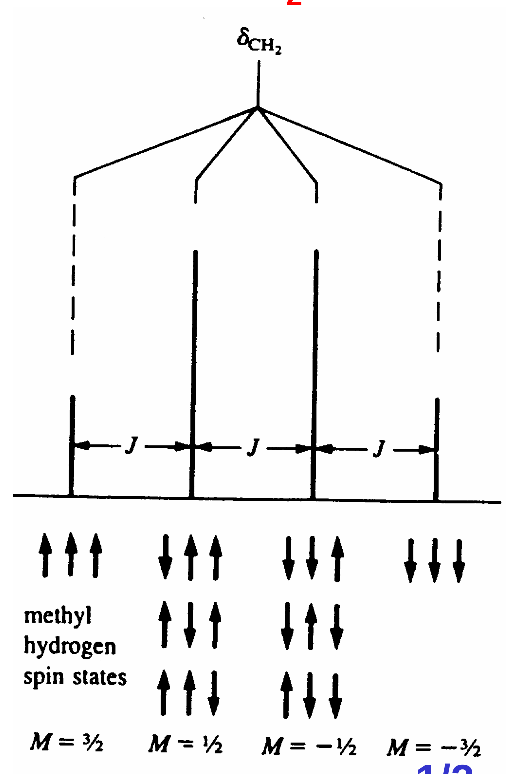
$M = m_1 + m_2 + m_3 + \ldots$

CH_3



+1/2 -1/2

CH_2



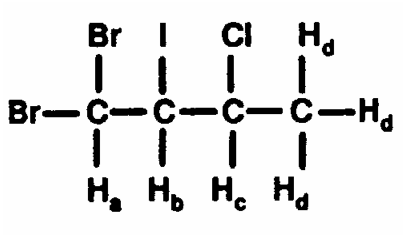
+1/2 -1/2

Proton Spin-Coupling: n+1 Rule

Pascal's Triangle

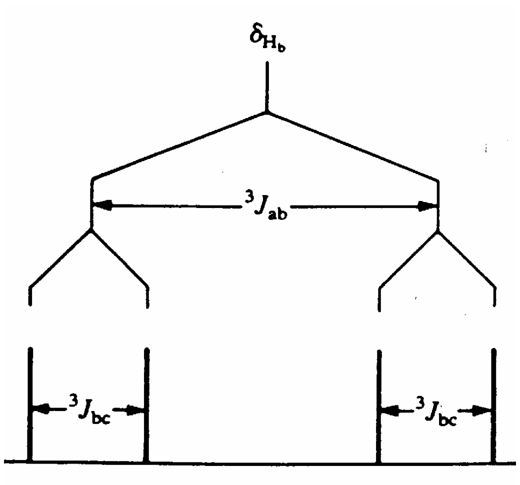
n	$n+1$	Intensity Ratio	Multiplicity	Multiplet
0	1	1	1	Singlet
1	2	1 1	2	Doublet
2	3	1 2 1	3	Triplet
3	4	1 3 3 1	4	Quartet
4	5	1 4 6 4 1	5	Quintet
5	6	1 5 10 10 5 1	6	Sextet

Proton Spin-Coupling and n+1 Rule



Hb

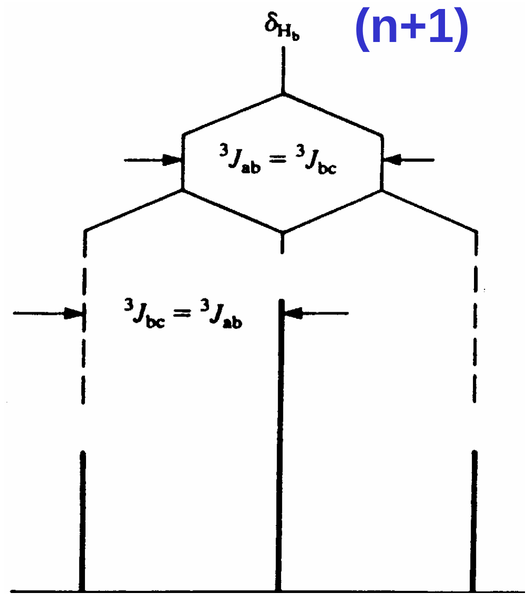
(n+1)(m+1)



$J_{ab} > J_{bc}$

Hb

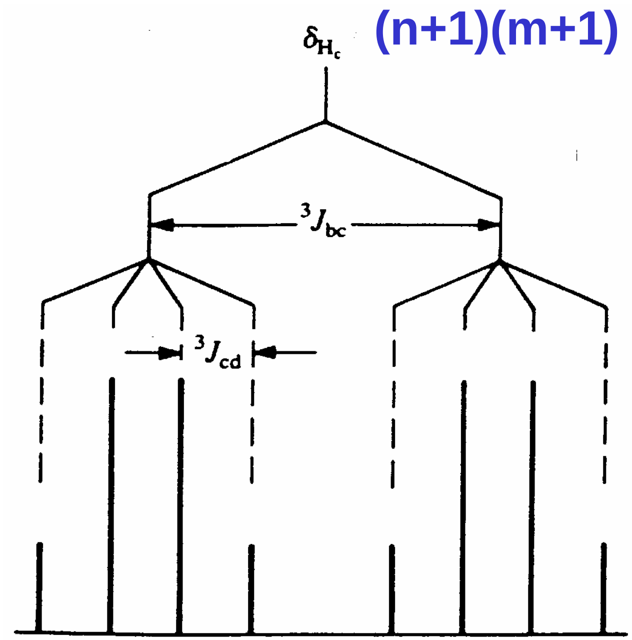
(n+1)



$J_{ab} = J_{bc}$

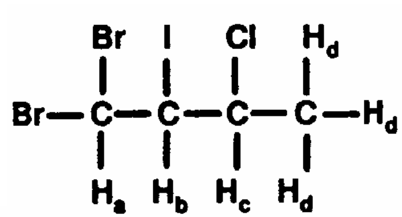
Hc

(n+1)(m+1)

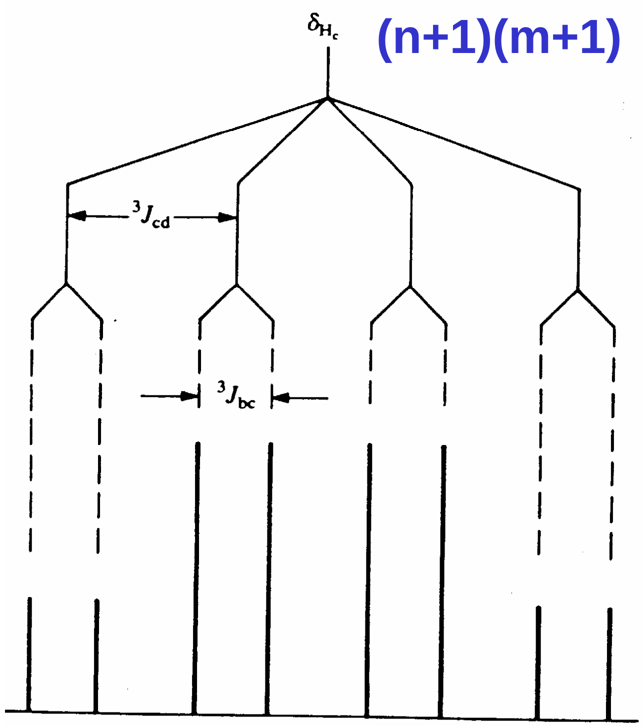


$J_{bc} > J_{cd}$

Proton Spin-Coupling and n+1 Rule

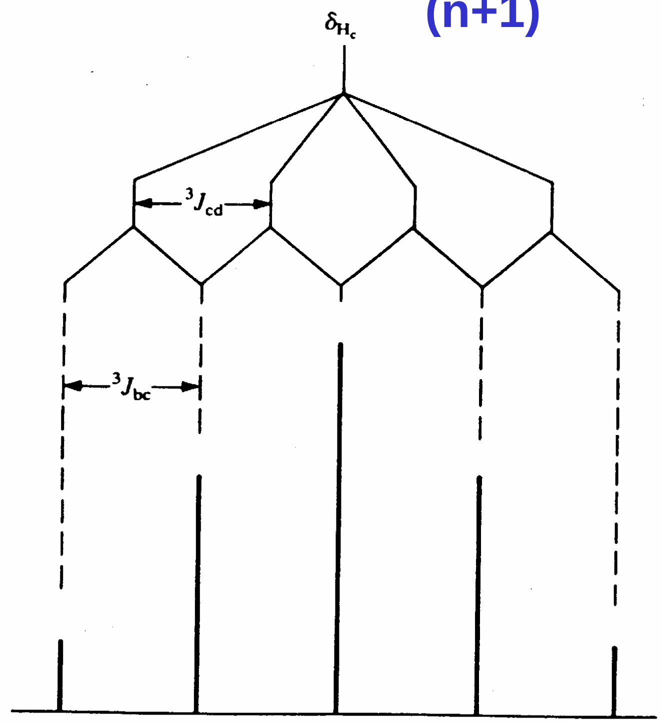


H$_c$ (n+1)(m+1)



$J_{bc} < J_{cd}$

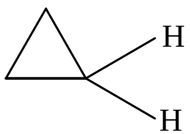
H$_c$ (n+1)



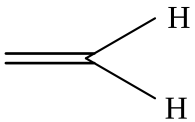
$J_{bc} = J_{cd}$

The Geminal Karplus Correlation

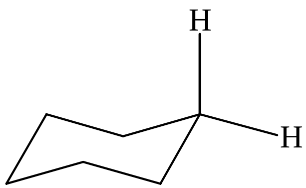
$^2J_{HH}$ for CH_2 Groups as a Function of H-C-H Angles



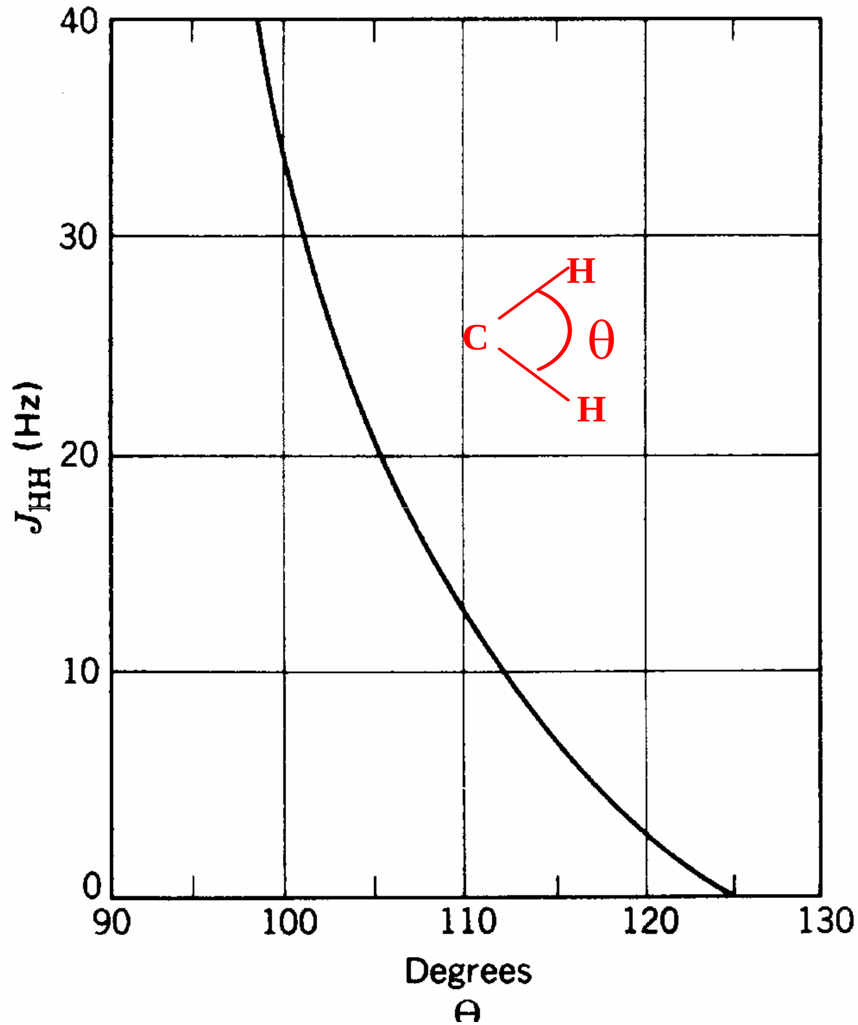
$^2J_{HH}$ 5 H_Z



$^2J_{HH}$ 0 – 3 H_Z

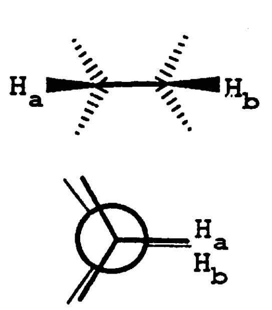


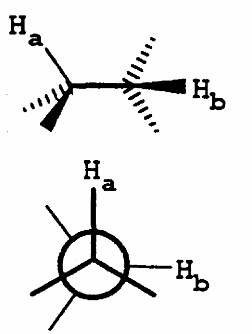
$^2J_{HH}$ 12 –18 H_Z

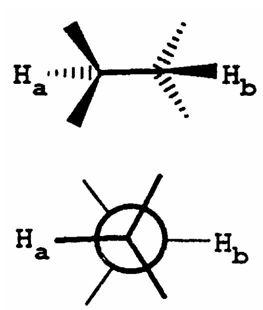


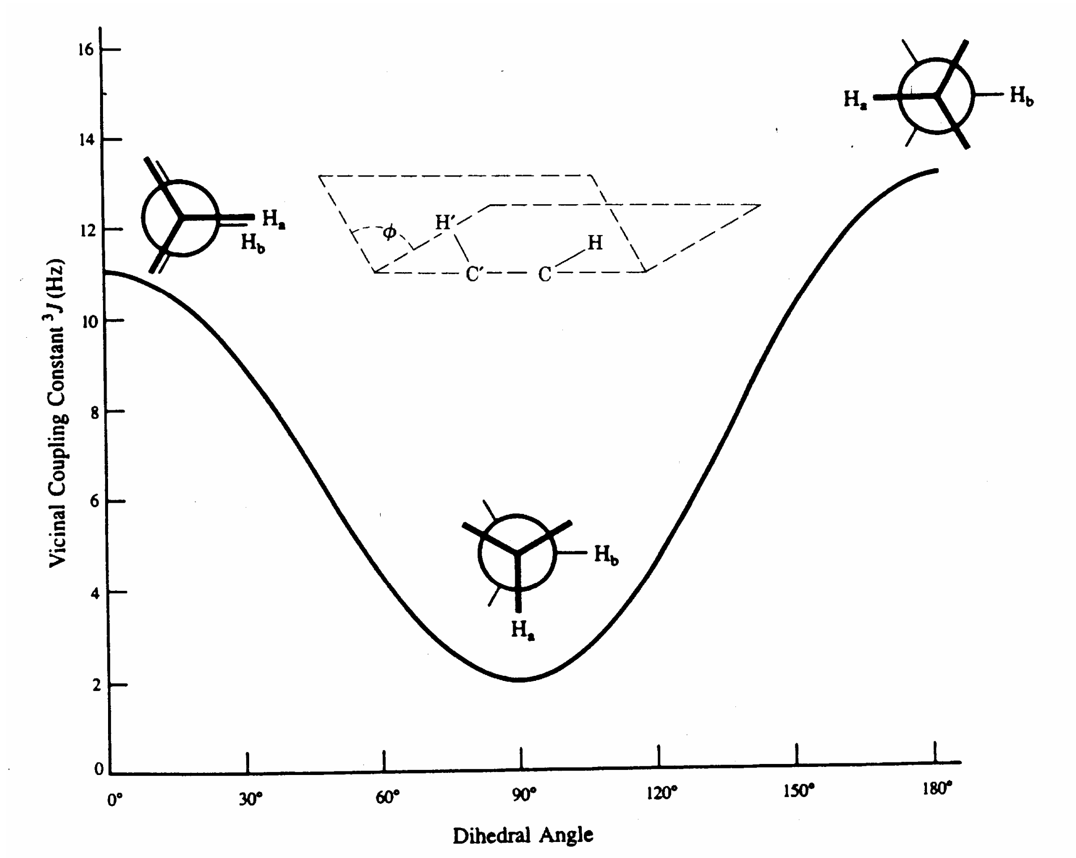
The Vincinal Karplus Correlation

Relationship between Dihedral Angle (Φ) and $^3J_{HH}$ Coupling Constants

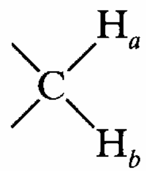
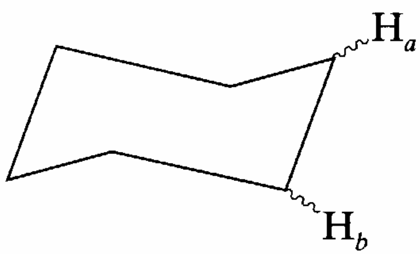




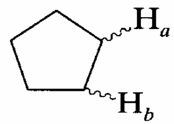
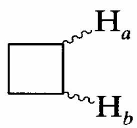
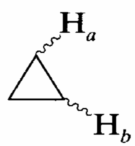
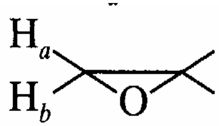
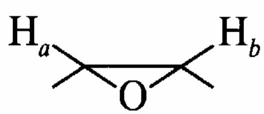
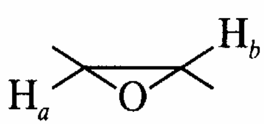




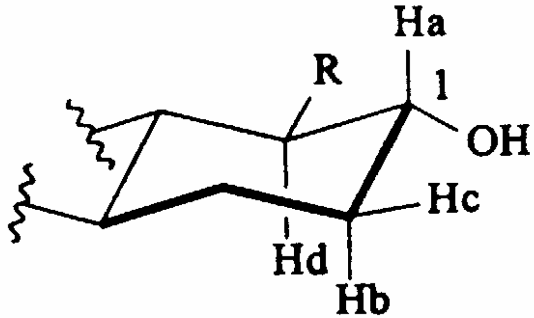
$^2J_{HH}$, $^3J_{HH}$ Coupling Constants of Alkanes

Type	J_{ab} (Hz)	J_{ab} Typical
	0–30	12–15
CH_a—CH_b (free rotation)	6–8	7
CH_a—C—CH_b ($^4J_{HH}$)	0–1	0
		
ax–ax	6–14	8–10
ax–eq	0–5	2–3
eq–eq	0–5	2–3

$^2J_{HH}$, $^3J_{HH}$ Coupling Constants of Alkanes

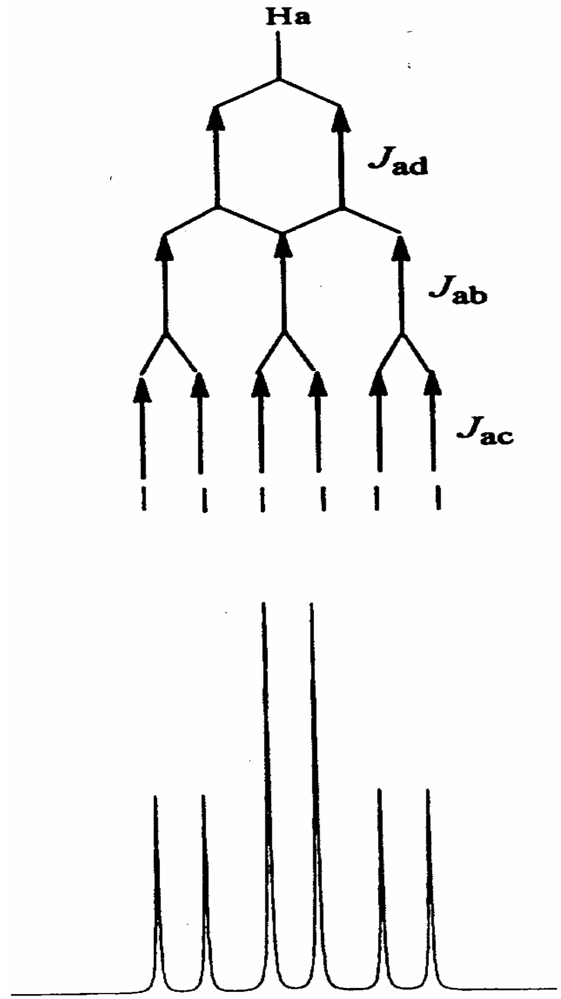
Type	J_{ab} (Hz)	J_{ab} Typical
 (cis or trans)	*cis* 5–10 *trans* 5–10	
 (cis or trans)	*cis* 4–12 *trans* 2–10	
 (cis or trans)	*cis* 7–13 *trans* 4–9	
		6
		4
		2.5

a-e Proton Couplings in Cyclic Compounds: Application of n+1 Rule

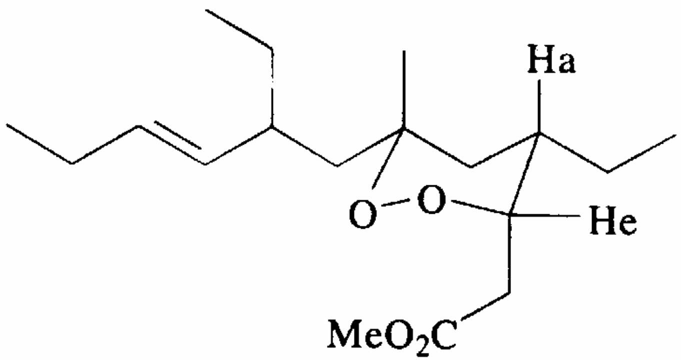


$J_{ab} = J_{ad} = 11$ Hz

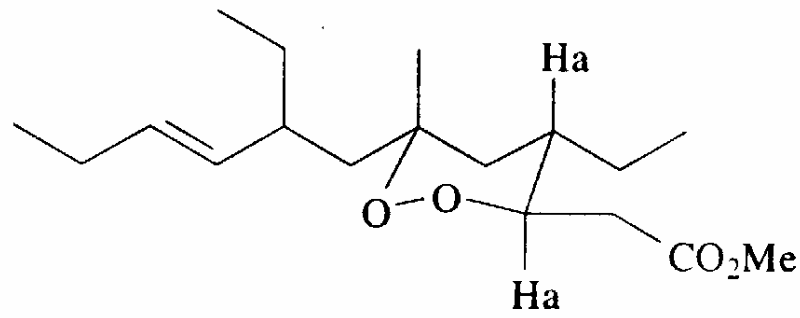
$J_{ac} = 4$ Hz



a-e Proton Couplings in Cyclic Compounds: Application of n+1 Rule

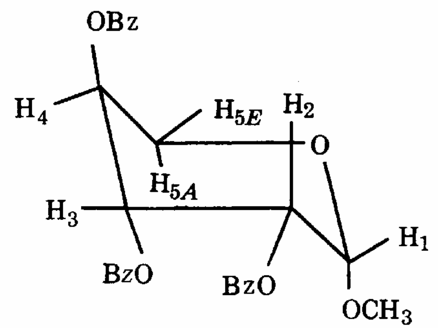


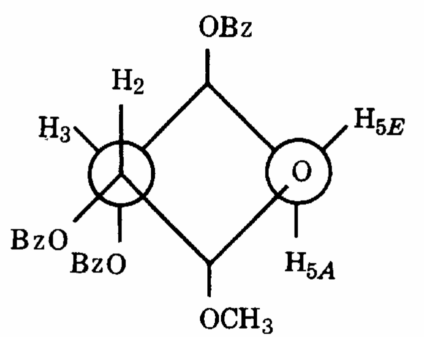
plakortin (**6a**)
$J_{ae} = 6$ Hz



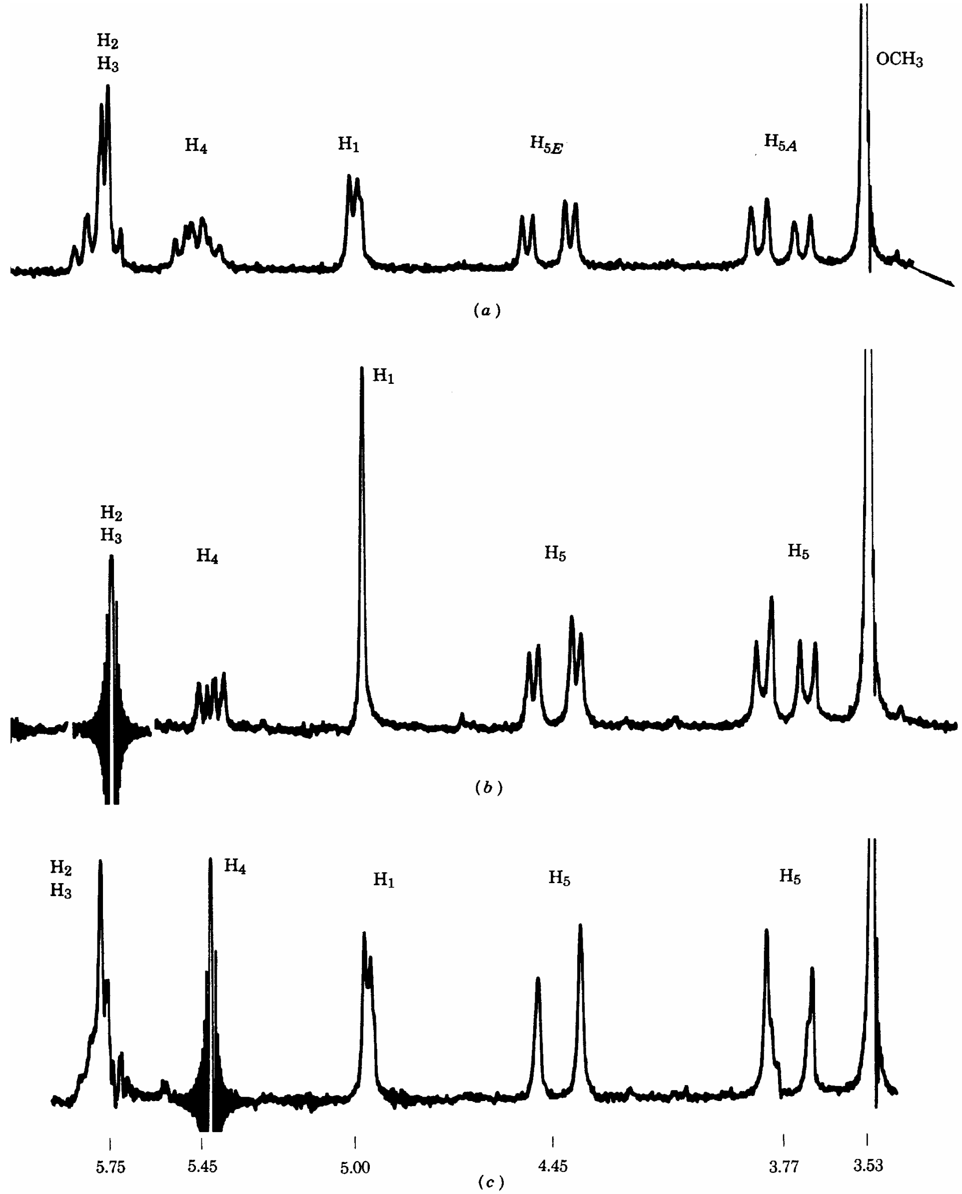
epiplakortin (**6b**)
$J_{aa} = 9$ Hz

a-e Proton Couplings in Cyclic Compounds: Application of n+1 Rule

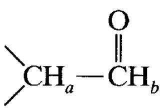
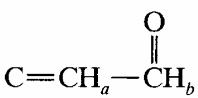
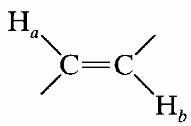
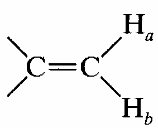
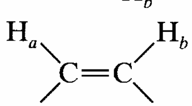
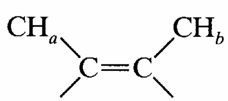
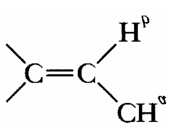


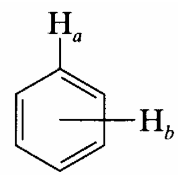
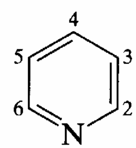
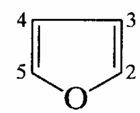
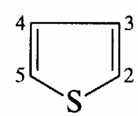


BzO = C_6H_5CO

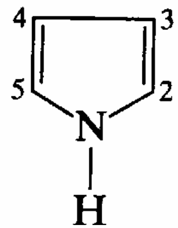
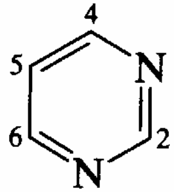
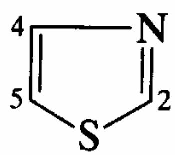


$^2J_{HH}$, $^3J_{HH}$ Coupling Constants of Unsaturated Compounds and Heteroaromatics

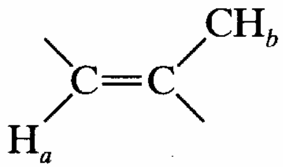
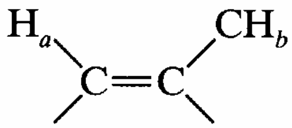
Type	J_{ab} (Hz)	J_{ab} Typical
CH_a—OH_b (no exchange)	4–10	5
	1–3	2–3
	5–8	6
	12–18	17
	0–3	0–2
	6–12	10
	0–3	1–2
	4–10	7

Type		J_{ab} (Hz)	J_{ab} Typical
	J (ortho)	6–10	9
	J (meta)	1–3	3
	J (para)	0–1	~0
	J (2–3)	5–6	5
	J (3–4)	7–9	8
	J (2–4)	1–2	1.5
	J (3–5)	1–2	1.5
	J (2–5)	0–1	1
	J (2–6)	0–1	~0
	J (2–3)	1.3–2.0	1.8
	J (3–4)	3.1–3.8	3.6
	J (2–4)	0–1	~0
	J (2–5)	1–2	1.5
	J (2–3)	4.9–6.2	5.4
	J (3–4)	3.4–5.0	4.0
	J (2–4)	1.2–1.7	1.5
	J (2–5)	3.2–3.7	3.4
$C=CH^a$—$CH^b=C$		9–13	10

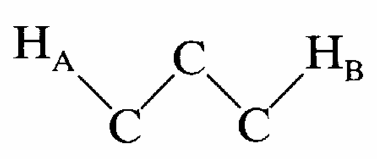
Spin-Coupling Constants of Heteroaromatics

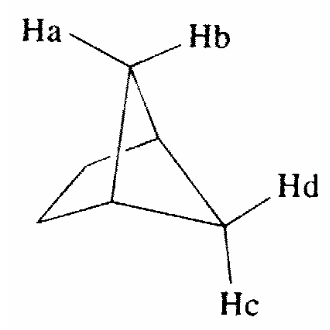
Type		J_{ab} (Hz)
	J (1–2)	2–3
	J (1–3)	2–3
	J (2–3)	2–3
	J (3–4)	3–4
	J (2–4)	1–2
	J (2–5)	1.5–2.5
	J (4–5)	4–6
	J (2–5)	1–2
	J (2–4)	0–1
	J (4–6)	2–3
	J (4–5)	3–4
	J (2–5)	1–2
	J (2–4)	~0

$^{n}J_{HH}$ Long Range Coupling

Type		J_{ab} (Hz)	J_{ab} Typical
	$^{4}J_{HH}$	0–3	1.5
	$^{4}J_{HH}$	0–3	2
$CH_a—C≡CH_b$	$^{4}J_{HH}$	2–3	
$—CH_a—C≡C—CH_b—$	$^{5}J_{HH}$	2–3	

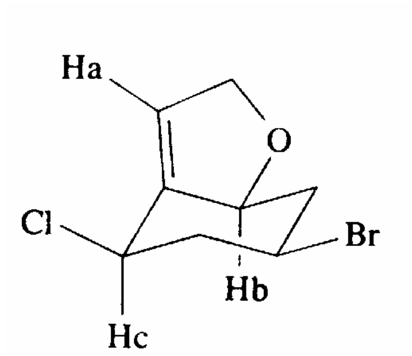
W-Type Long-Range Coupling



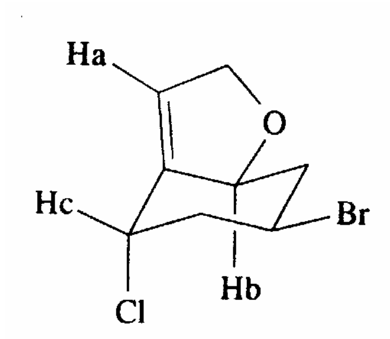


$^{4}Jac = 0.5$ Hz

$^{4}Jad = {}^{4}Jbc = 0$Hz

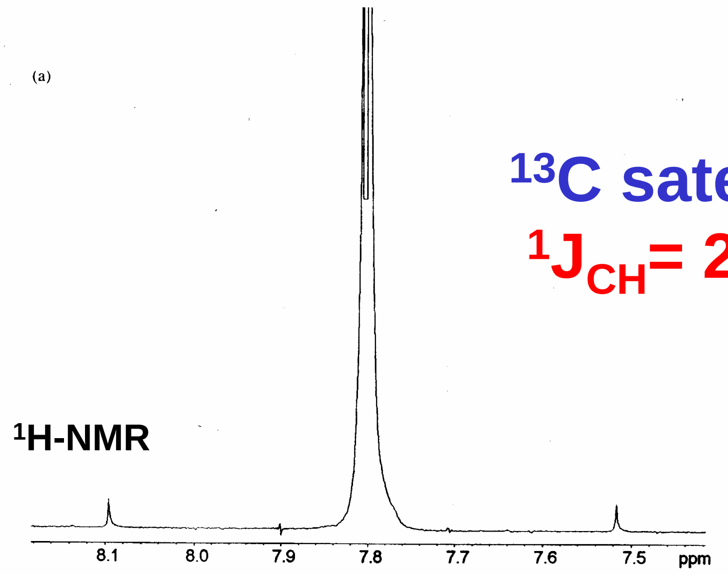


$J_{ab} = 2$ Hz, $J_{bc} = 2$ Hz

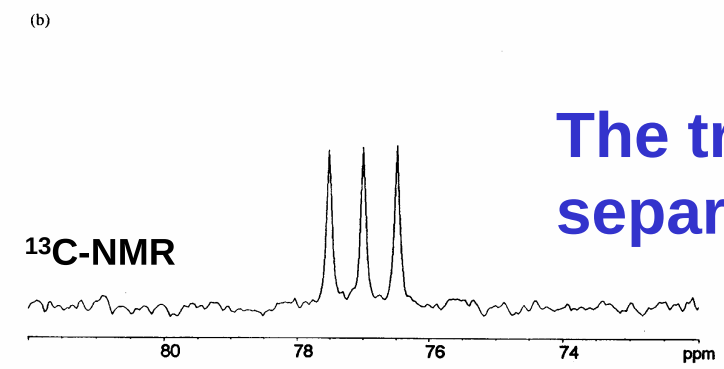


$J_{ab} = 2$ Hz, $J_{bc} = 0$ Hz

1H-NMR-^{13}C Spin-Coupling



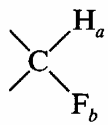
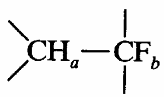
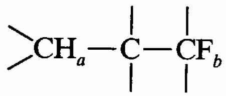
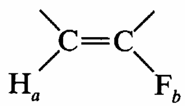
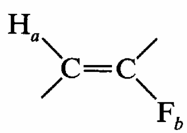
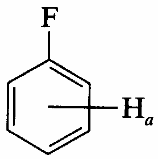
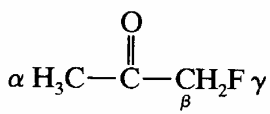
^{13}C satellites separated by $^1J_{CH}$= 210Hz



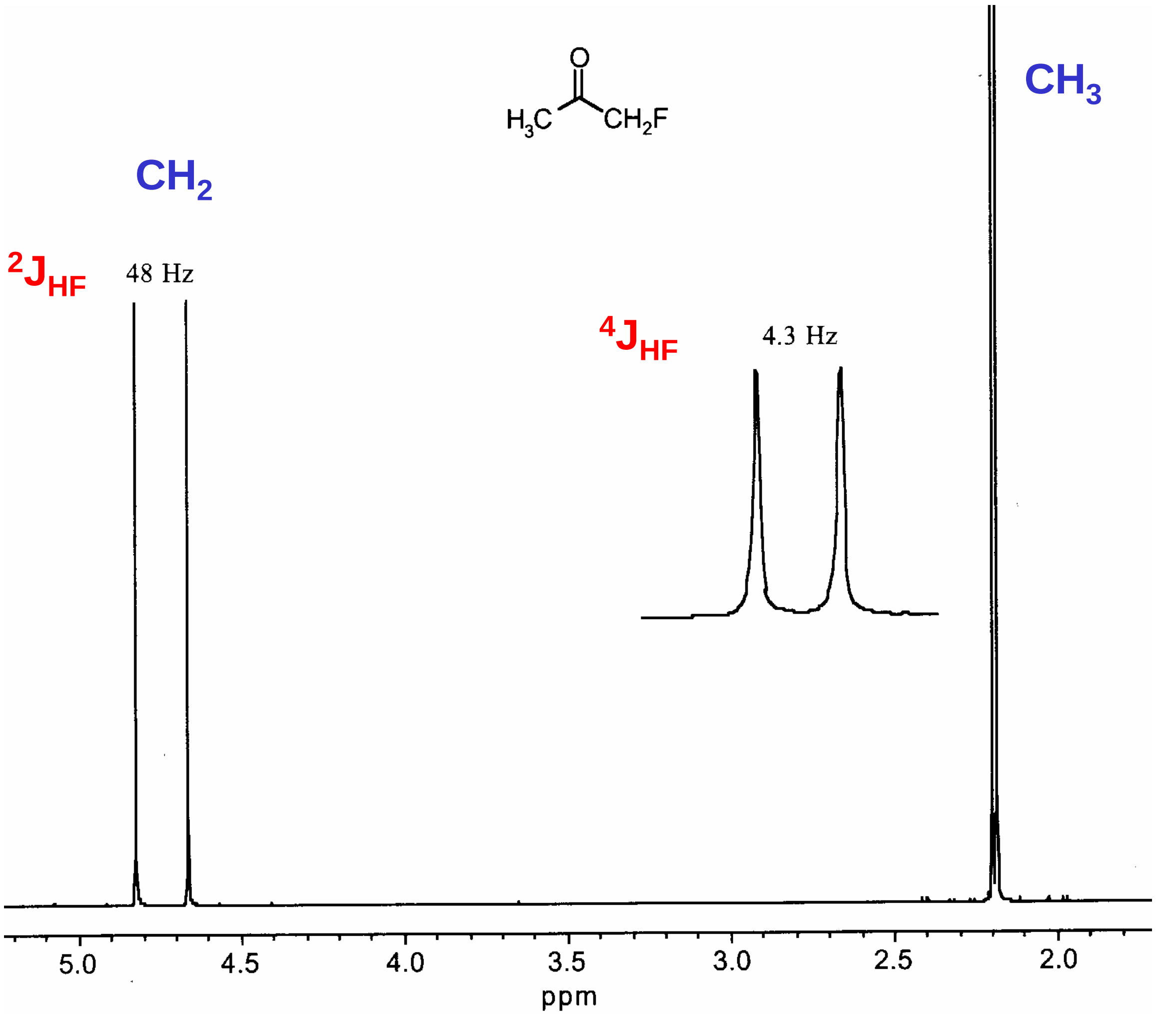
The triplet ^{13}C peaks of $CDCl_3$ separated by $^1J_{CD}$ = 32Hz

H-^{19}F Spin-Coupling Constant

^{19}F I =1/2

Type	J_{ab} (Hz)	J_{ab} Typical
Proton–Fluorine		
	$^2J_{HF}$	44–81
	$^3J_{HF}$	3–25
		0–4
		1–8
		12–40
		*o* 6–10 *m* 5–6 *p* 2
		$\alpha\gamma$ 4.3 $\beta\gamma$ 48

H-^{19}F Spin-Coupling



^{1}H spectrum of fluoroacetone in $CDCl_3$ at 300 MHz.

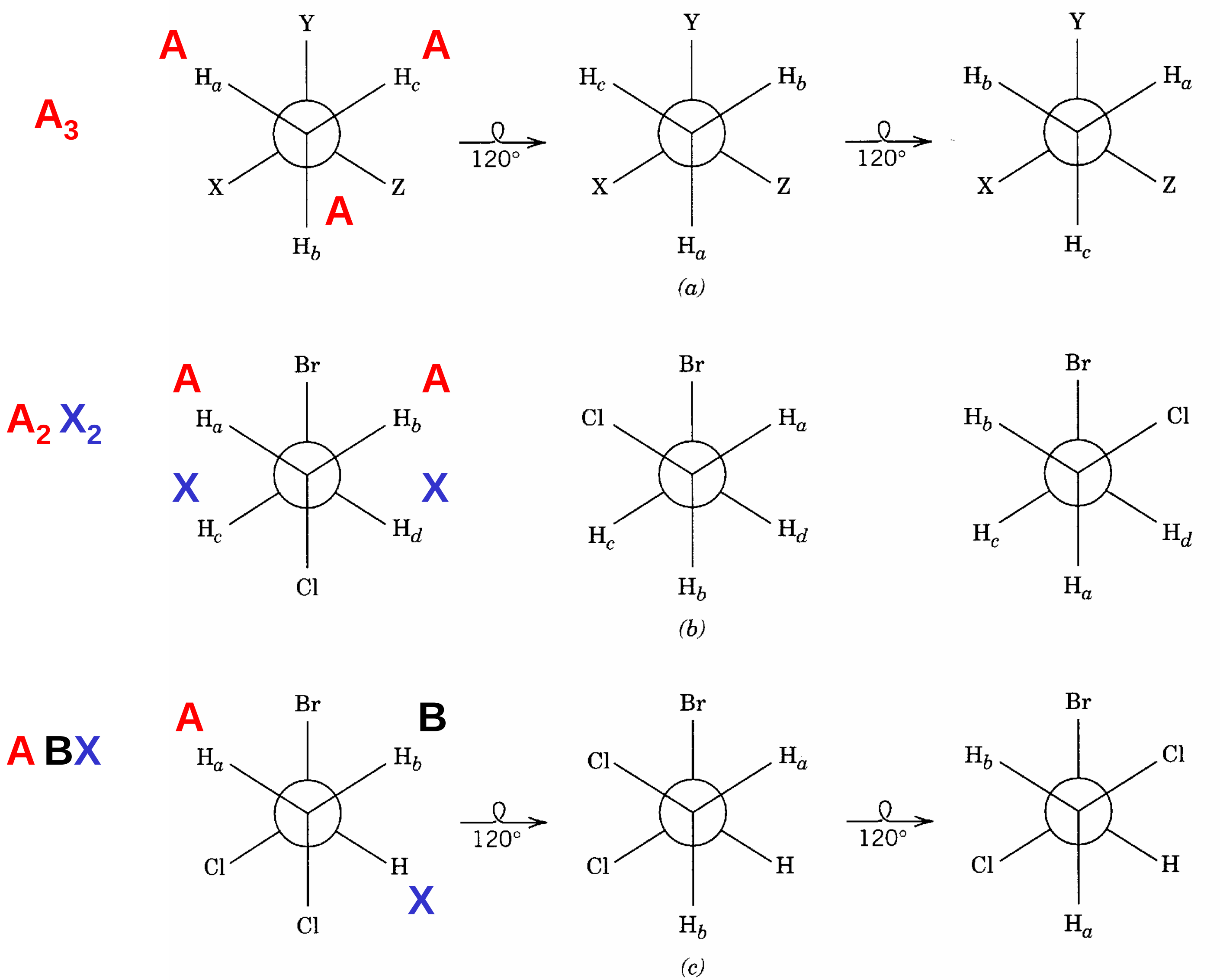
H- ^{31}P Spin-Coupling Constant

^{31}P I =1/2

Type		J_{ab} (Hz)	J_{ab} Typical
Proton–Phosphorus			
$>P(=O)H$	$^{1}J_{HP}$	630–707	
$(CH_3)_3P$	$^{2}J_{HP}$	2.7	
$(CH_3)_3P{=}O$		13.4	
$(CH_3CH_2)_3P$		0.5 (HCCP)	13.7 (HCP)
$(CH_3CH_2)_3P{=}O$		11.9 (HCCP)	16.3 (HCP)
$CH_3P(=O)(OR)_2$		10–13	
$CH_3C{-}P(=O)(OR)_2$	$^{3}J_{HP}$	15–20	
$CH_3OP(OR)_2$		10.5–12	
$P[N(CH_3)_2]_3$		8.8	
$O{=}P[N(CH_3)_2]_3$		9.5	

Chemical Shift Equivalence and Inequivalence

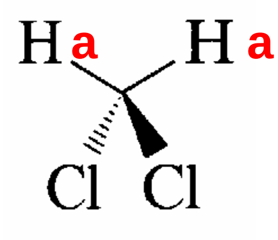
Newman projections of three staggered rotamers



Chemical Shift Equivalence

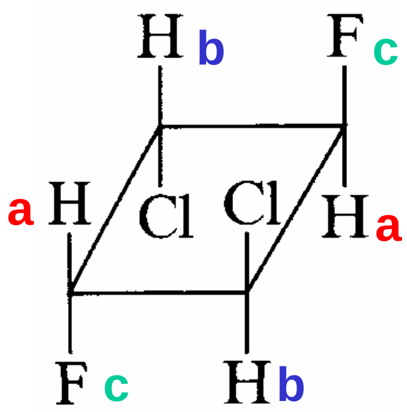
a. Homotropic protons by C_2

(axis of symmetry)



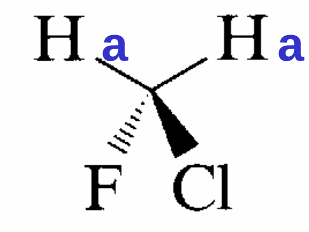
b. Enantiotropic protons by *i*

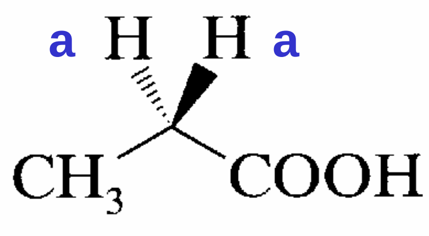
(center of symmetry)



c. Enantiotropic protons by σ

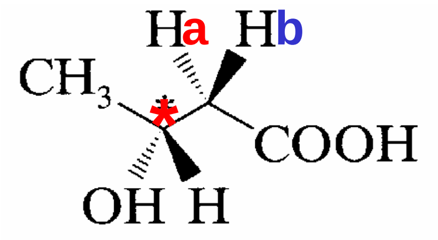
(plan of symmetry, mirror image)



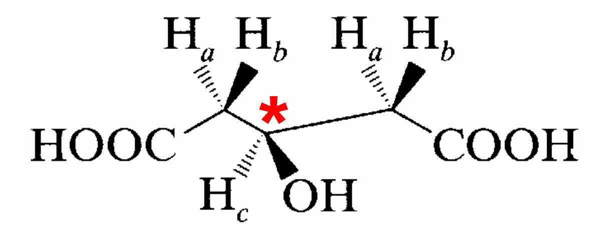


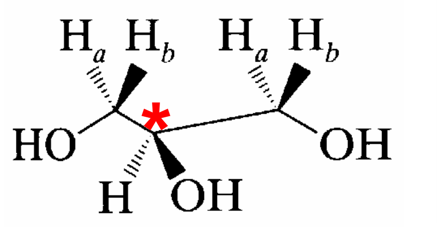
Chemical Shift Inequivalence

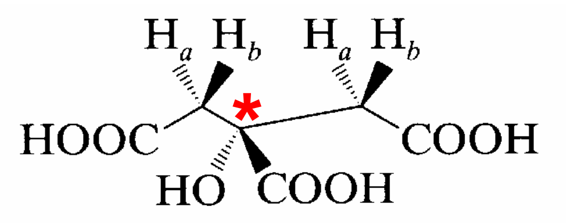
a. Diastereotopic proton in a chiral molecule

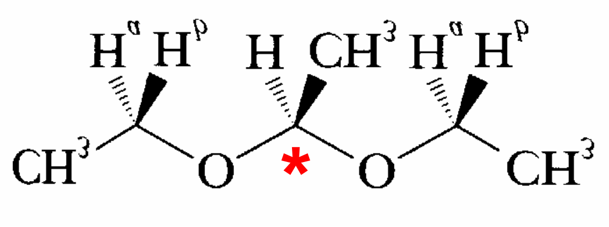


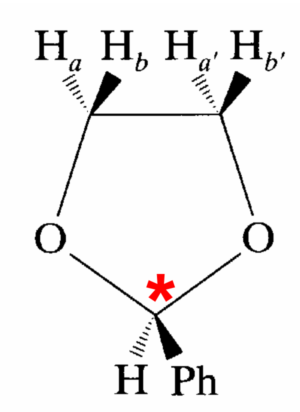
b. Diastereotopic proton in a achiral molecules







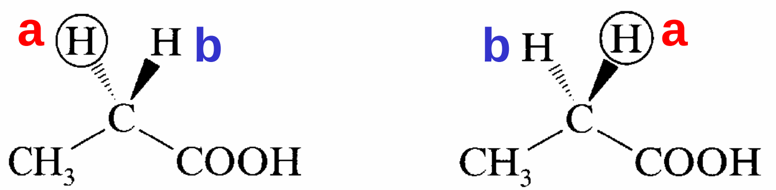




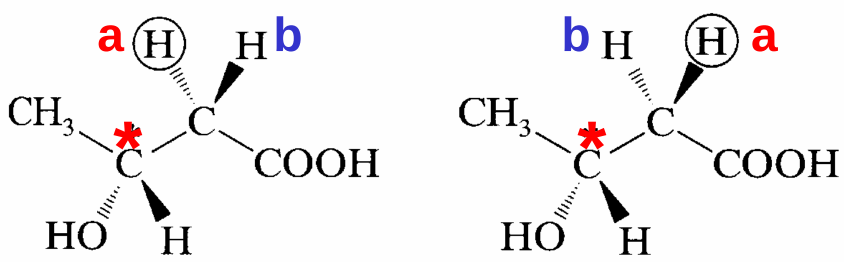
Chemical Shift Inequivalence



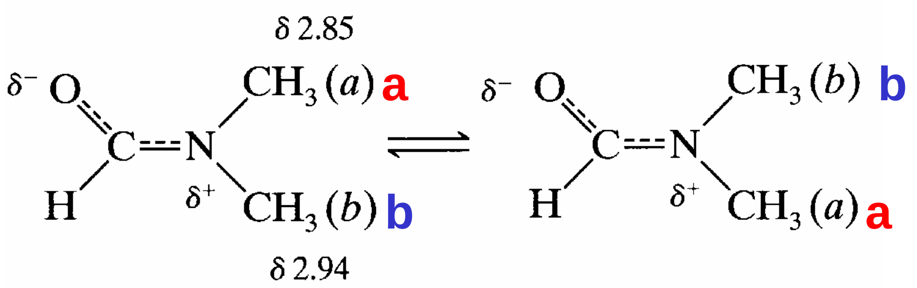
Equivalent molecules



Enantiomers



Diastereomers



Partial double bond property

Chemical Shift Equivalence and Magnetic Equivalence

Chemical shift equivalence:

$\Delta\nu_{AB} / J_{AB} > 6$

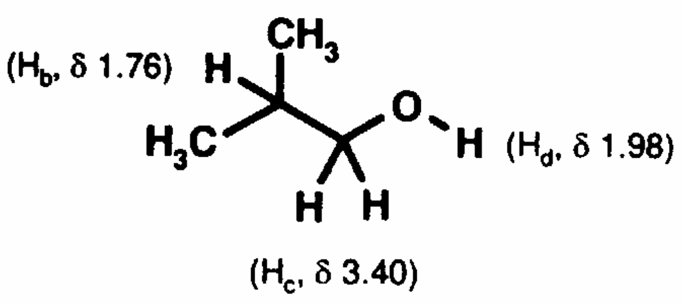
$\delta A = \delta B$

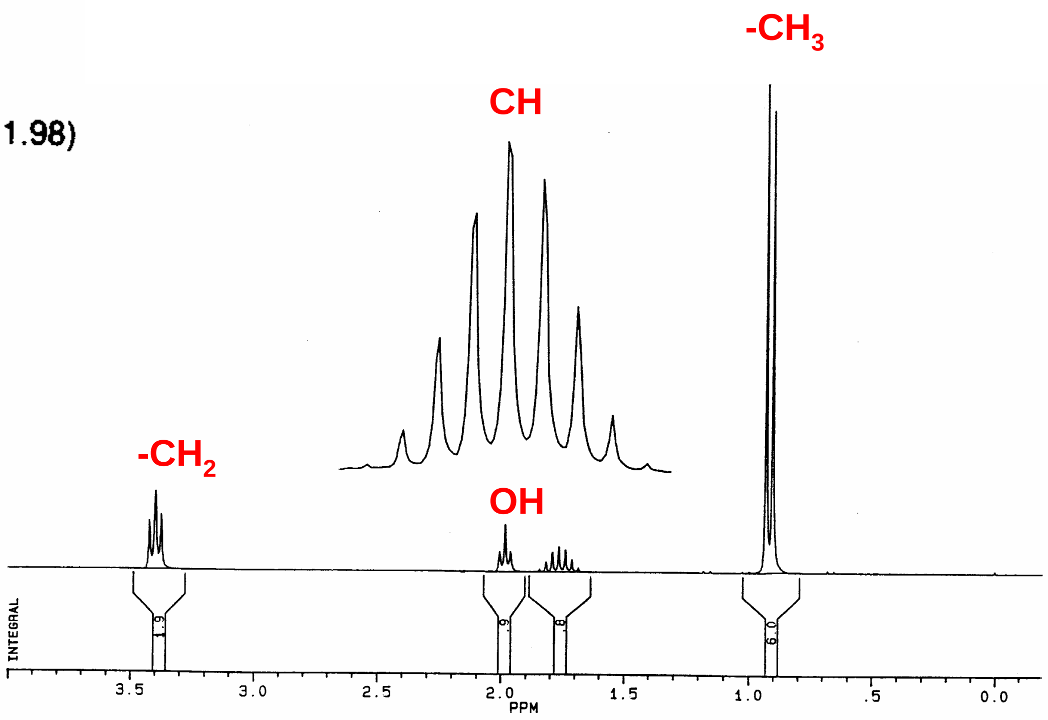
magnetic equivalence:

$\Delta\nu_{AB} / J_{AB} > 6$

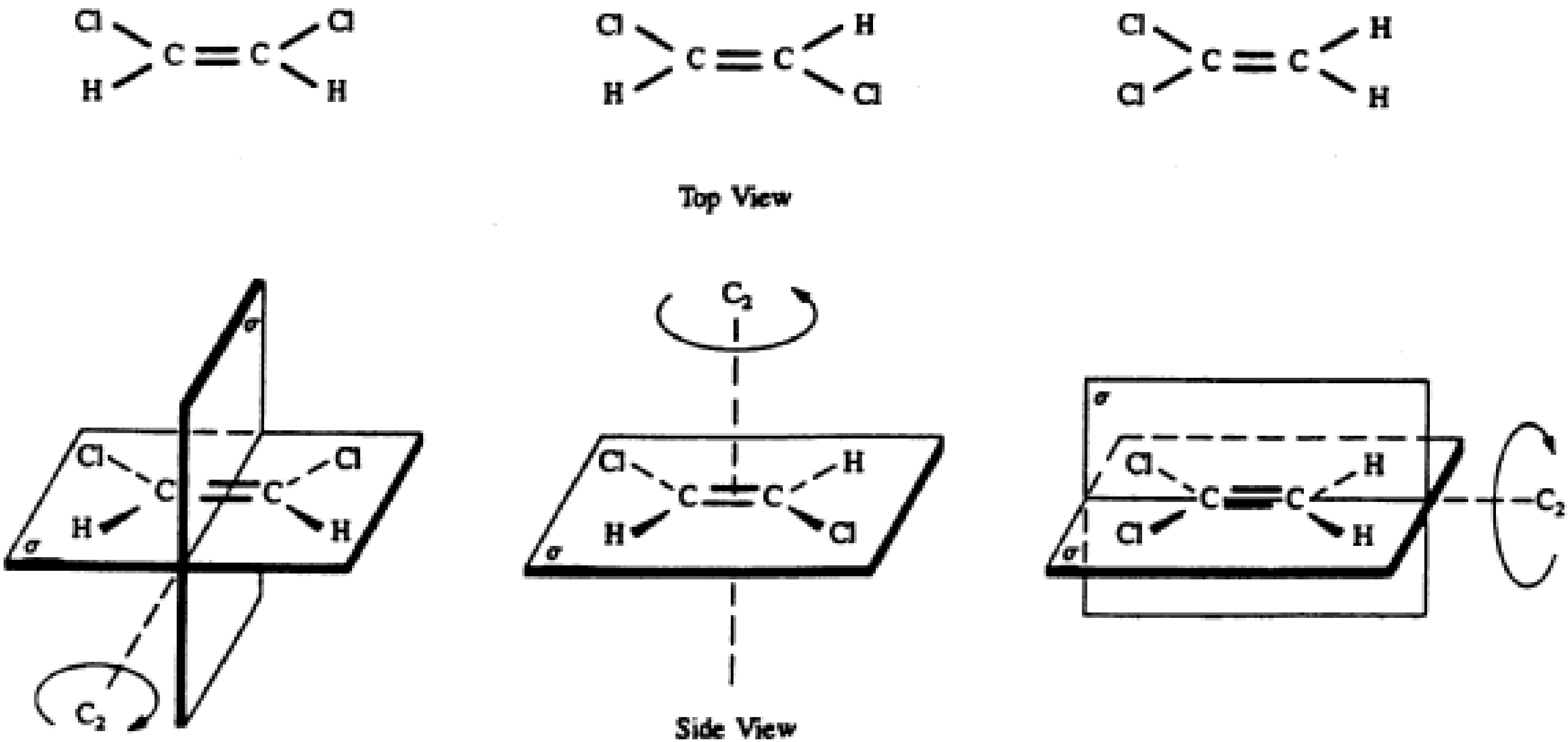
$\delta A = \delta B$

$J_{AB} = J_{BA}$

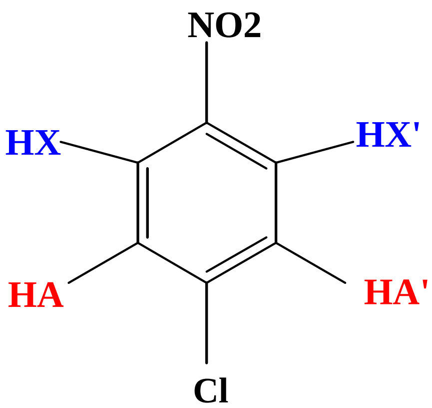


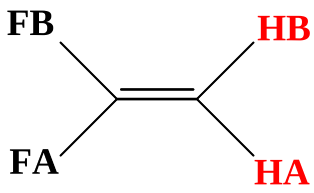


Chemical Shift Equivalence and Magnetic Equivalence

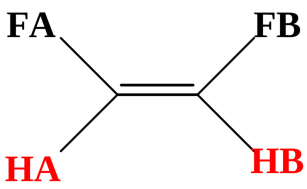


Chemical Shift Equivalence and Magnetic Inequivalence

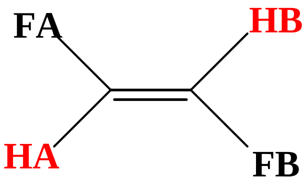




J_{AB} ~ 2 Hz



J_{AB} ~ 10 Hz



J_{AB} ~ 16 Hz

$\delta A = \delta A'$

$\delta X = \delta X'$

$J_{AX} = J_{A'X'}$ 7-10 Hz

$J_{A'X} = J_{AX'}$ 1 Hz

$\delta A = \delta B$

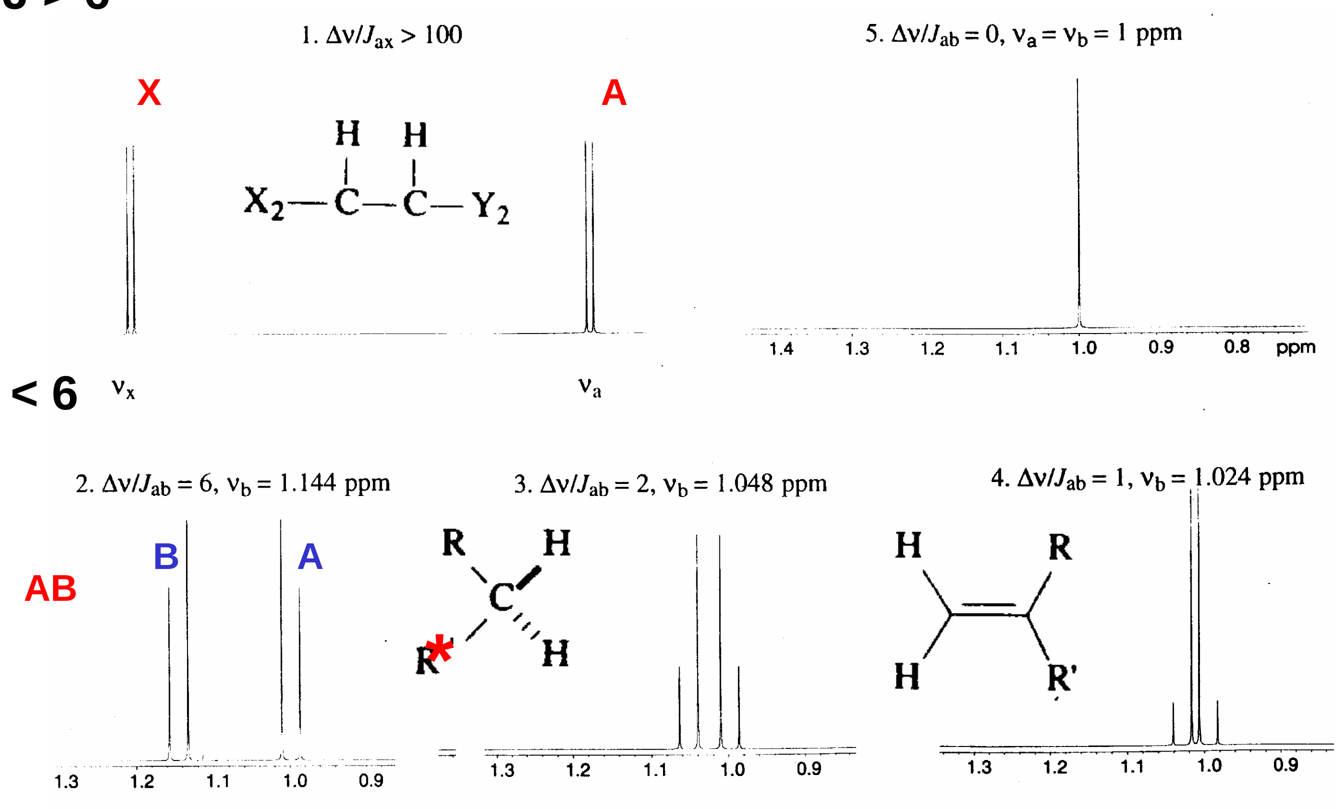
$J_{AB} \neq J_{AF} \neq J_{BF}$

Multipletes for Various Types of Spin Systems

Two Spin Systems (AX to AB)

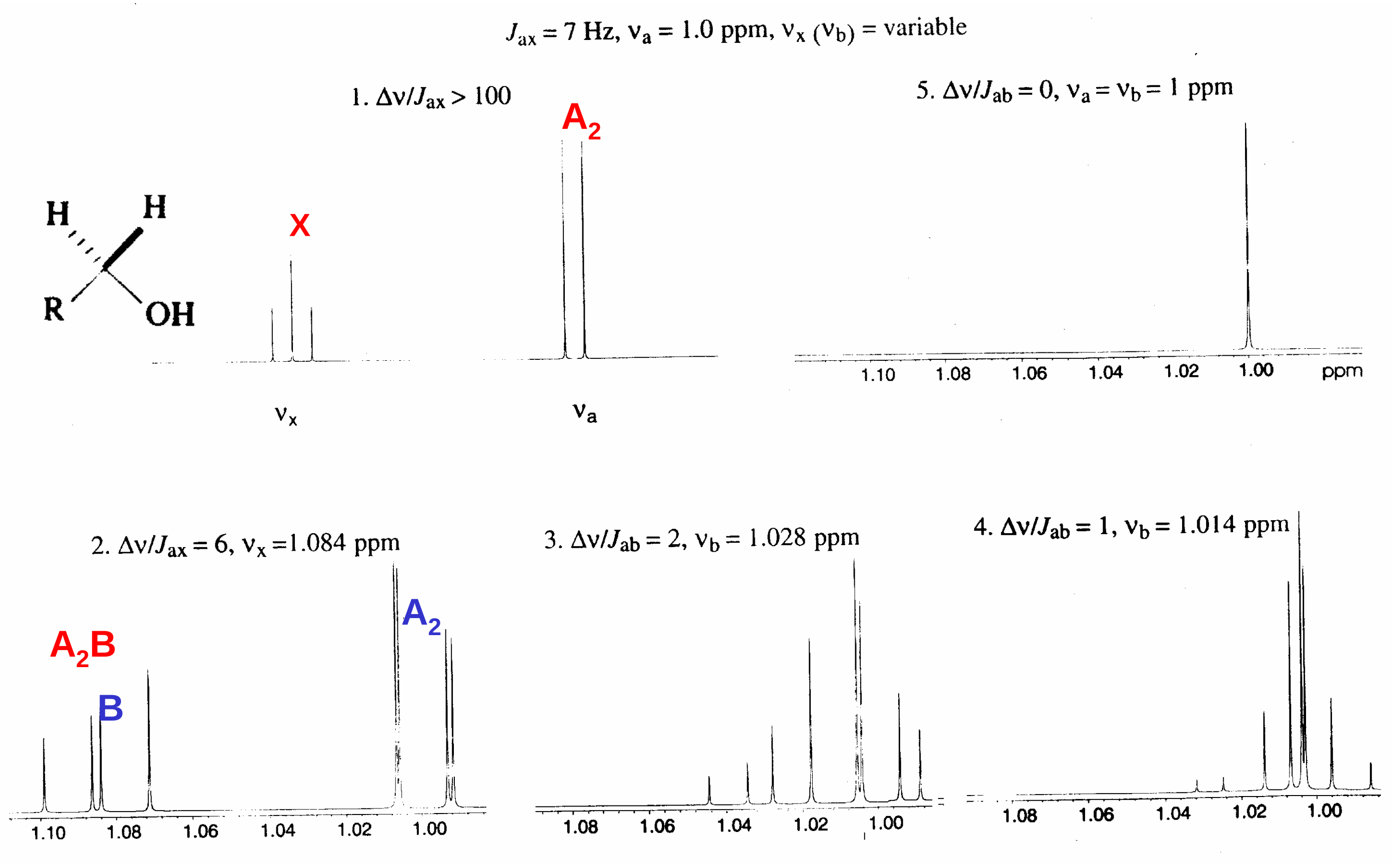
$\Delta\nu$ /J > 6

$\Delta\nu$ /J < 6

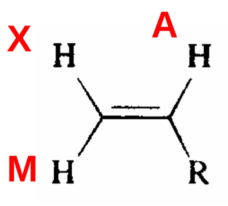


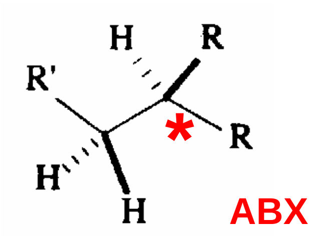
Multipletes for Various Types of Spin Systems

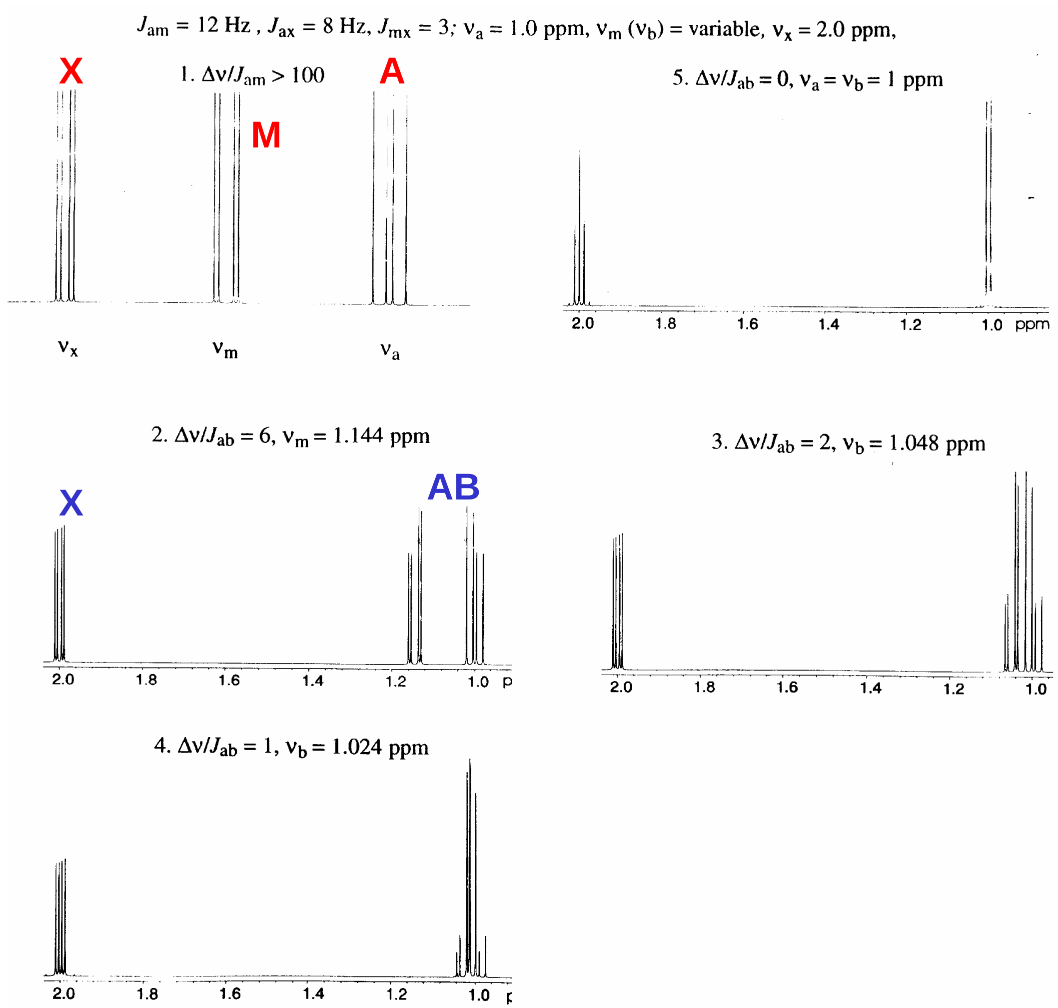
Three Spin Systems (A_2X to A_2B)



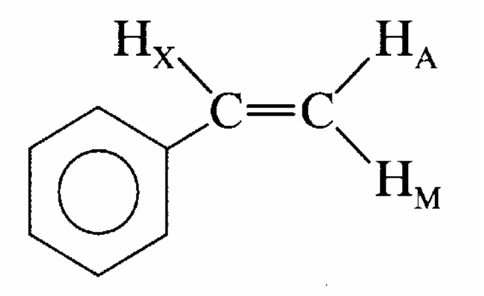
Three Spin Systems AMX to ABX

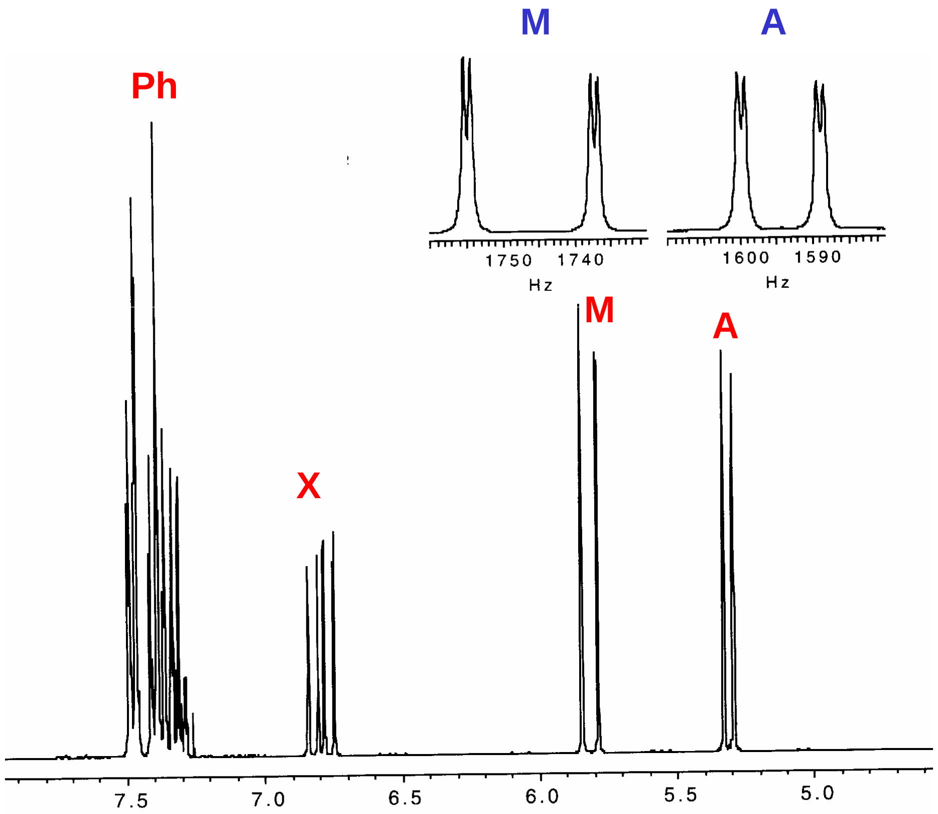






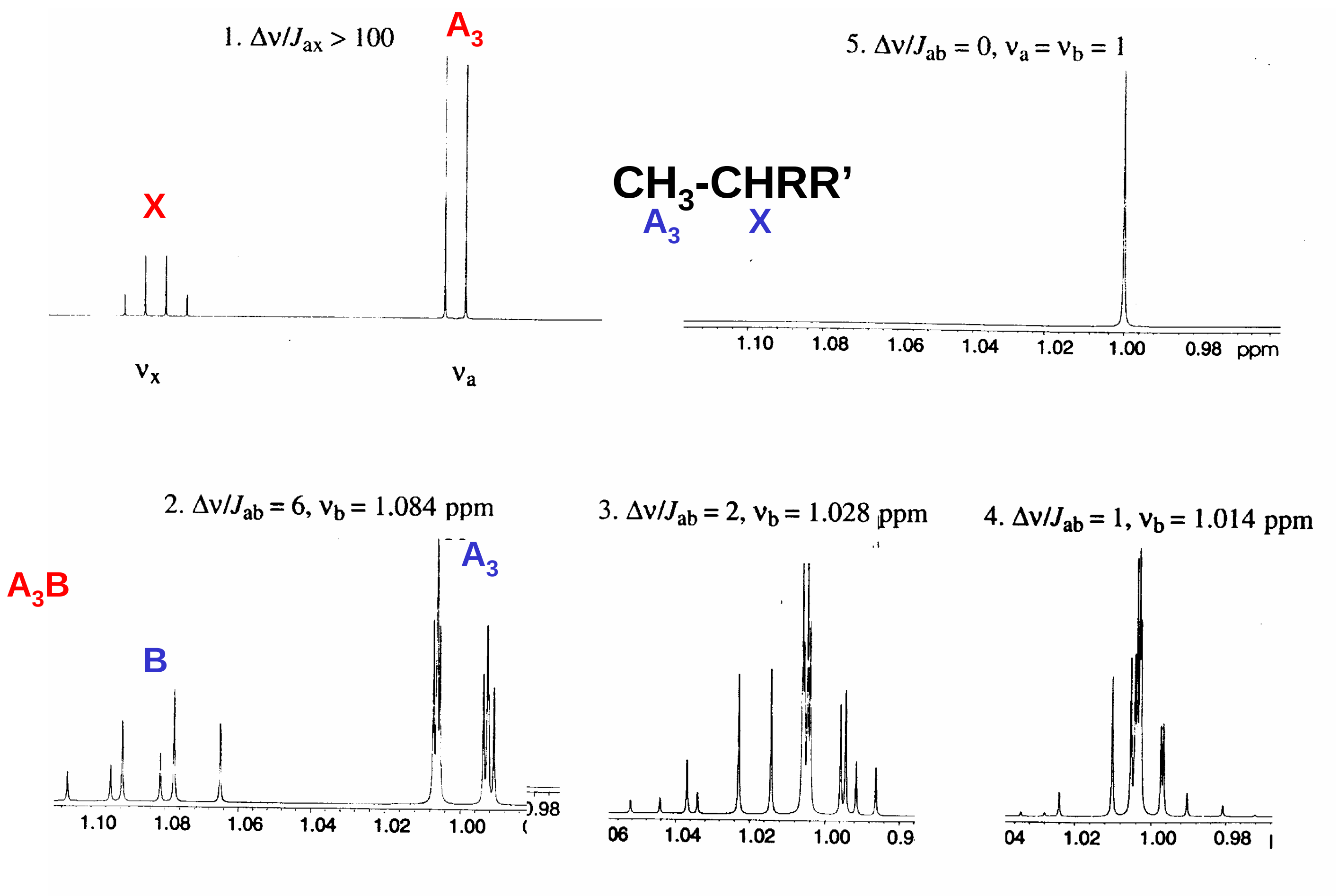
Three Spin Systems AMX to ABX





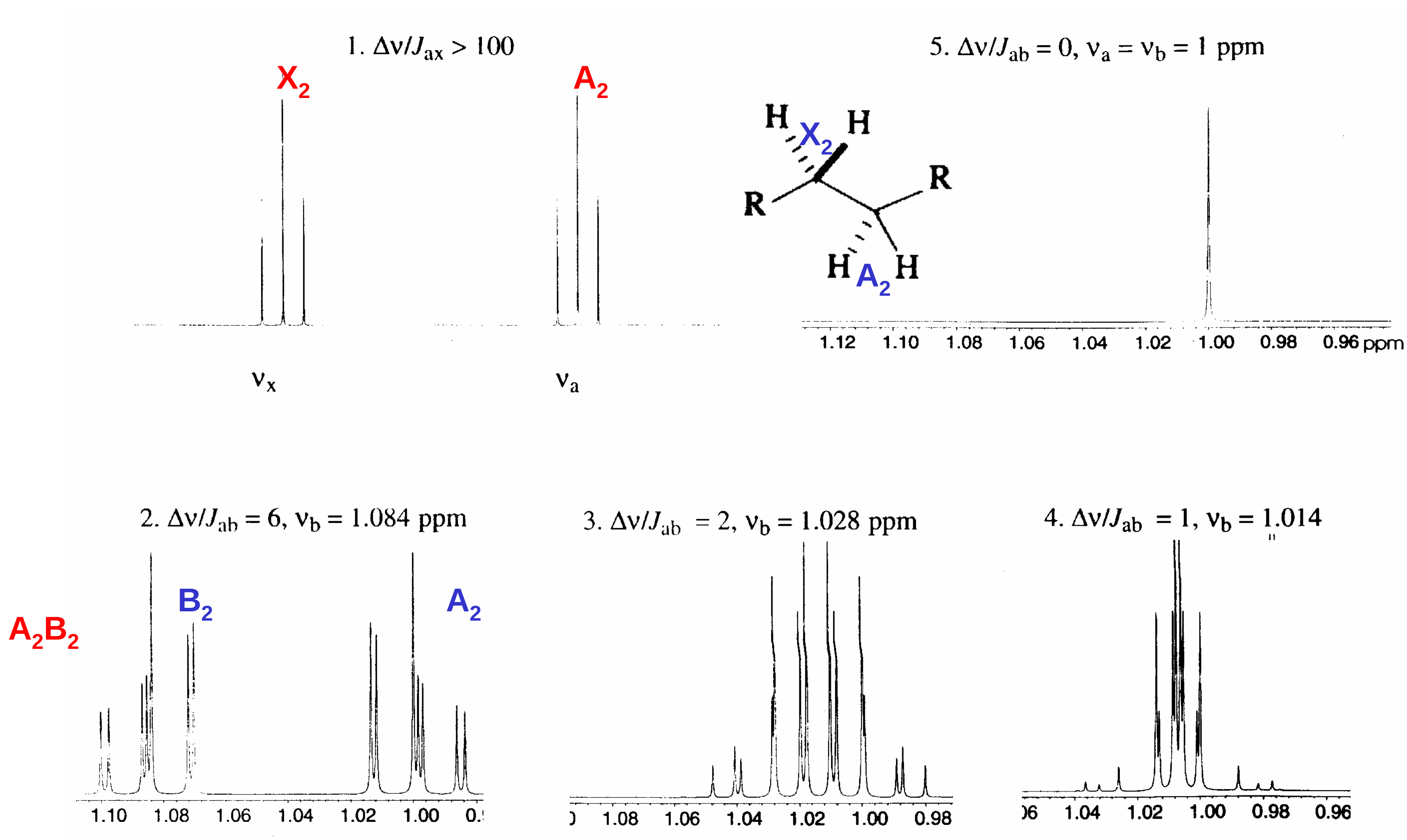
Multipletes for Various Types of Spin Systems

Four Spin Systems (A_3X to A_3B)



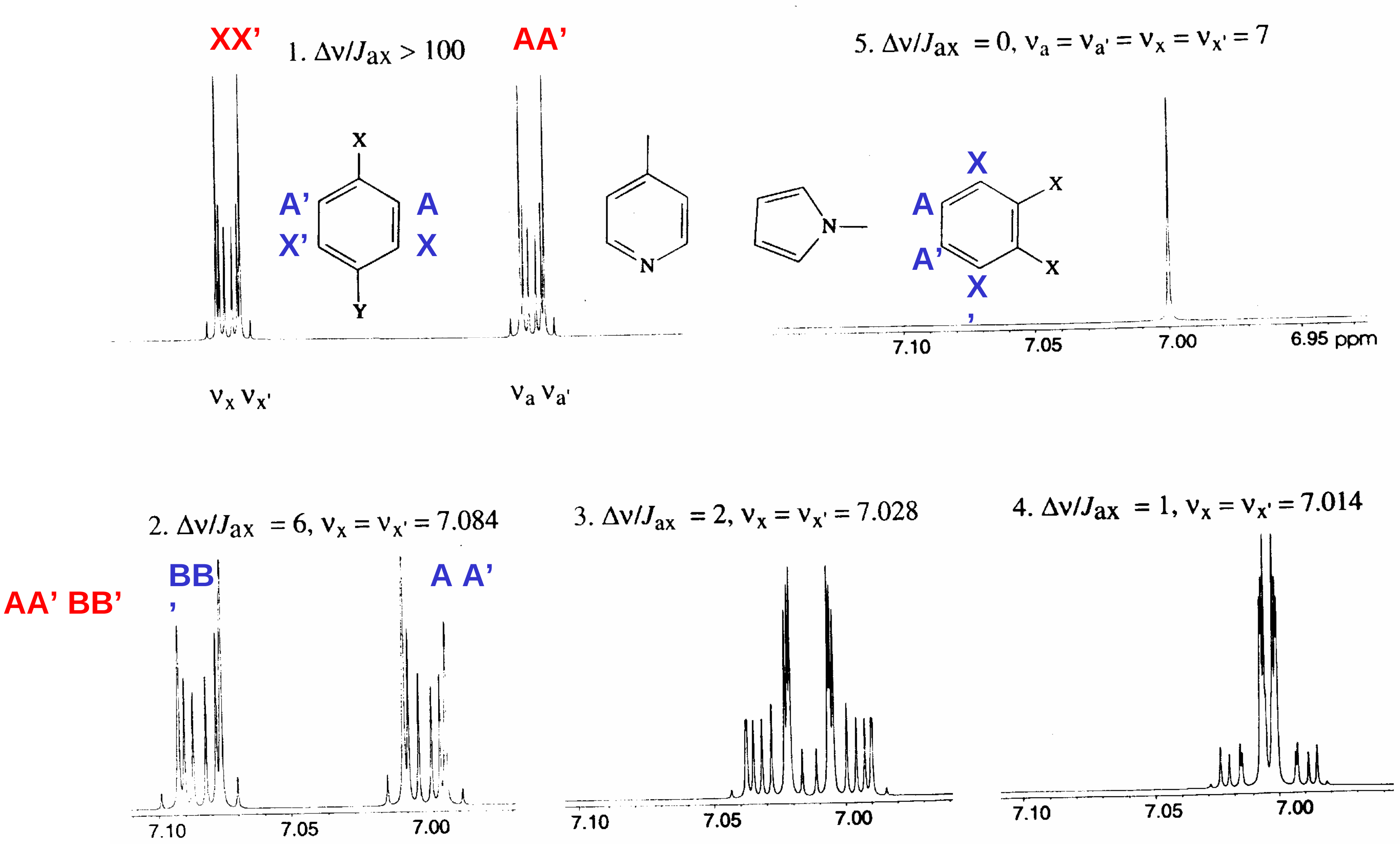
Multipletes for Various Types of Spin Systems

Four Spin Systems (A_2X_2 to A_2B_2)

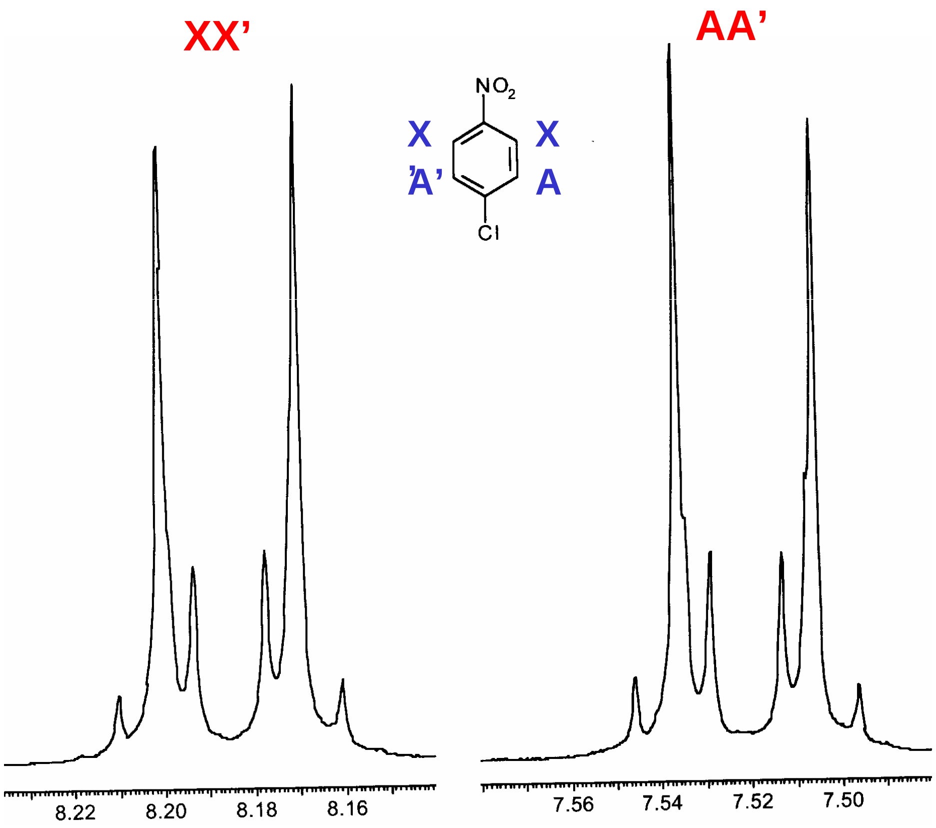


Multipletes for Various Types of Spin Systems

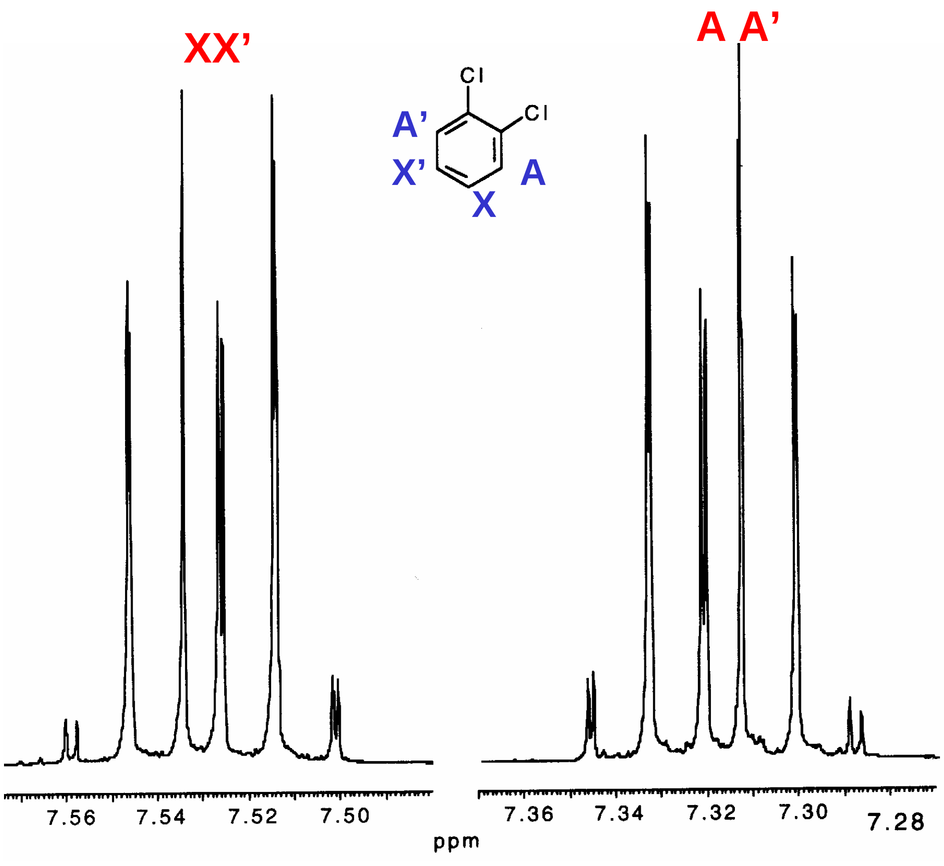
Four Spin Systems (AA’ XX’ to AA’ BB’)



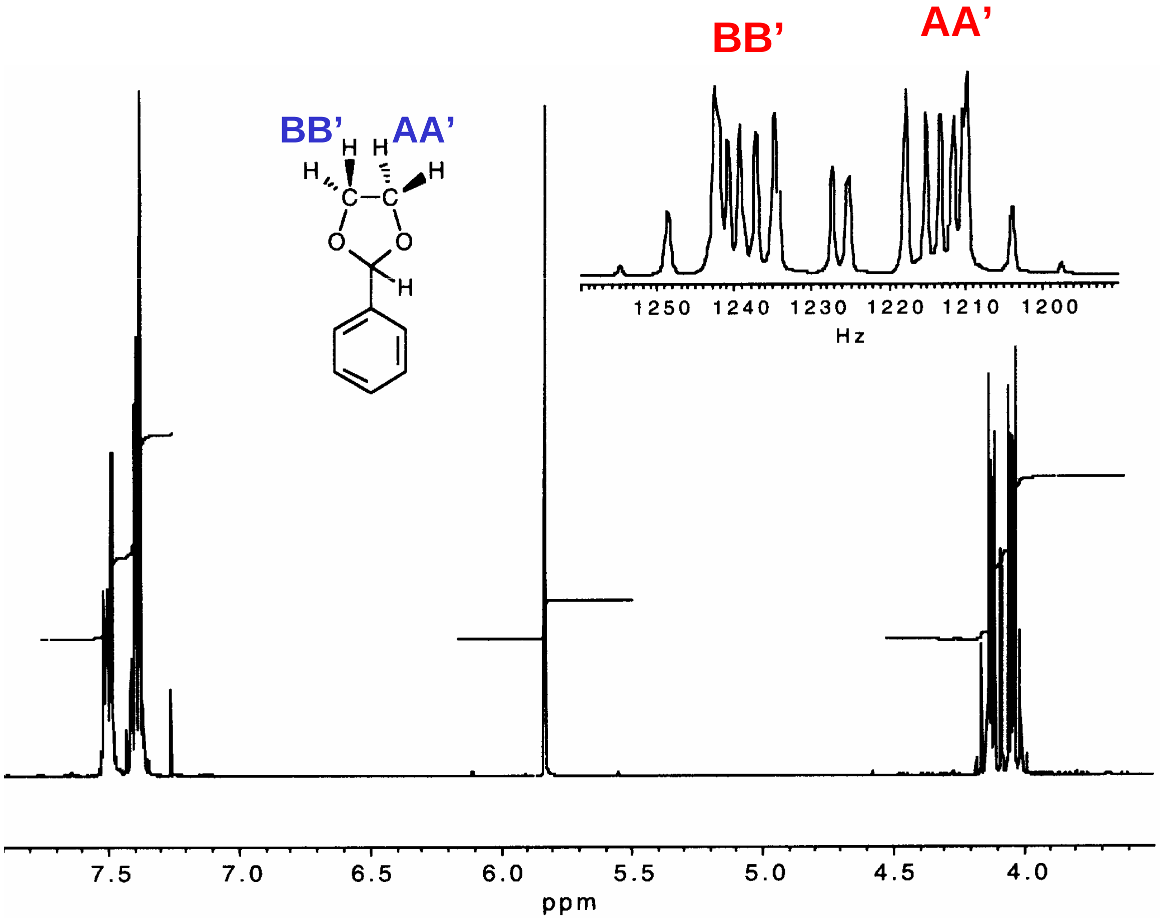
Four Spin Systems AA’ XX’



Four Spin Systems AA' XX'

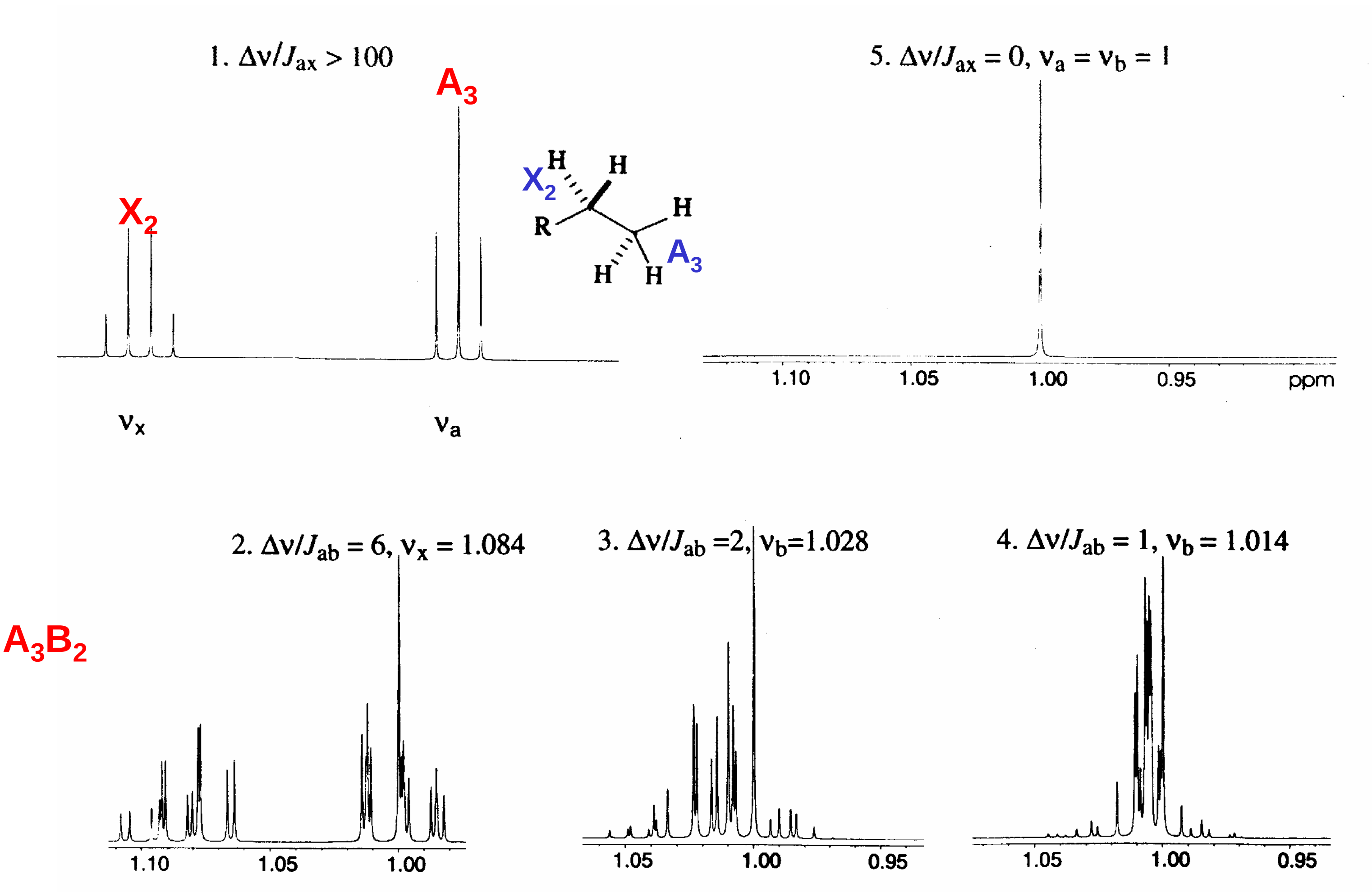


Four Spin Systems AA' BB'

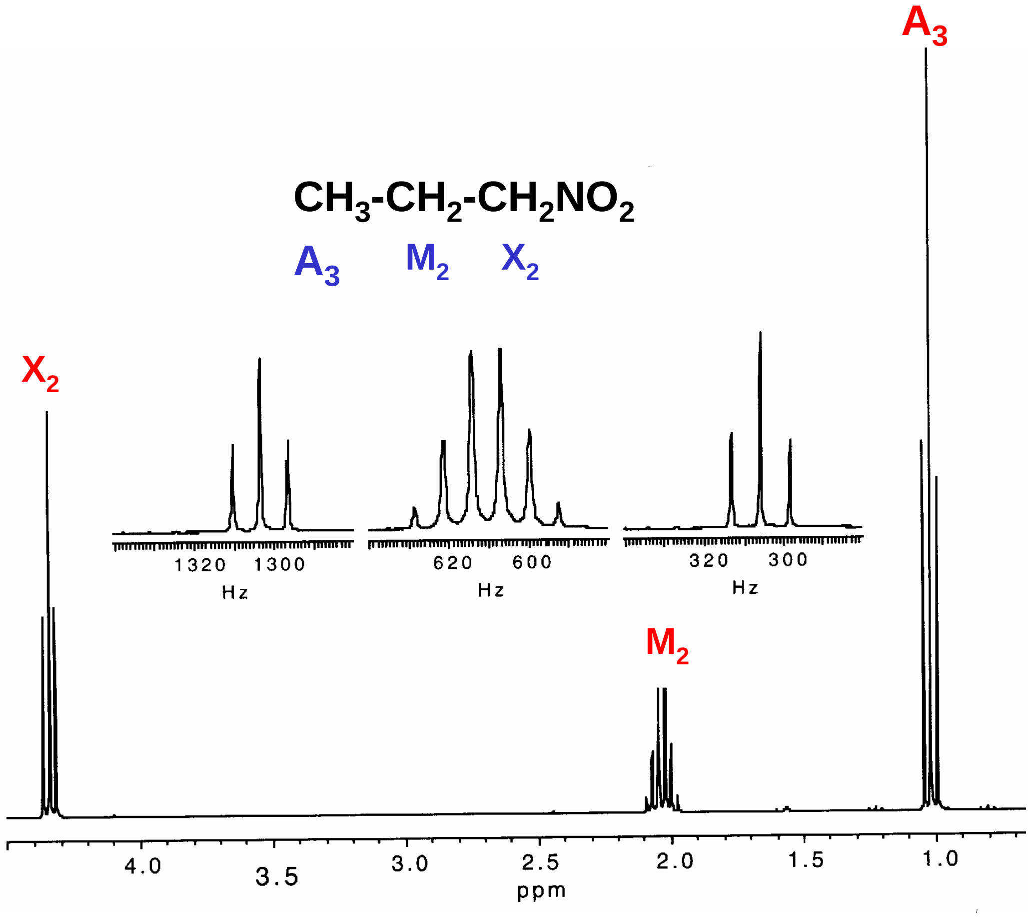


Multipletes for Various Types of Spin Systems

Five Spin Systems (A_3X_2 to A_3B_2)



Conformationally Mobile, Open-Chain Systems. Unsymmetrical Chains $A_3M_2X_2$

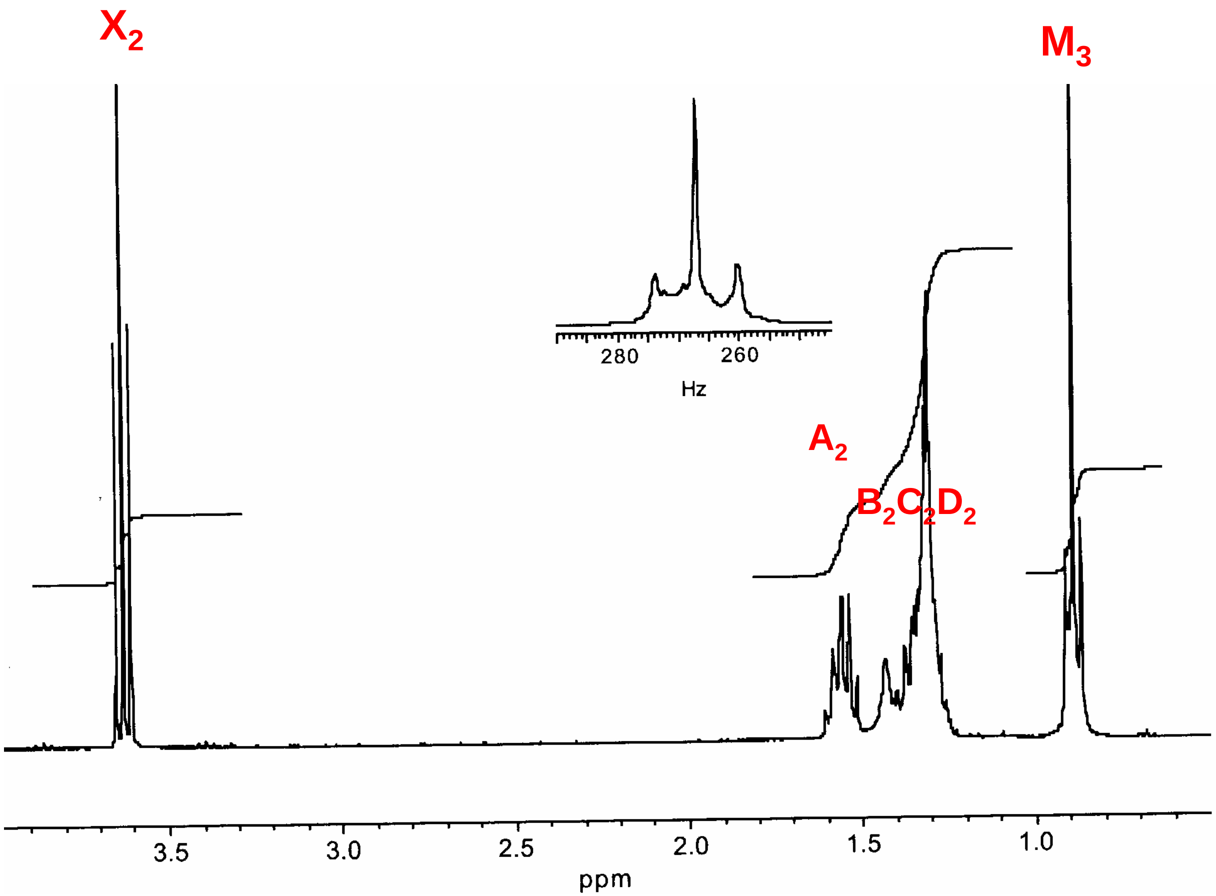


Conformationally Mobile, Open-Chain Systems.

Unsymmetrical Chains $A_2B_2C_2D_2M_3X_2$

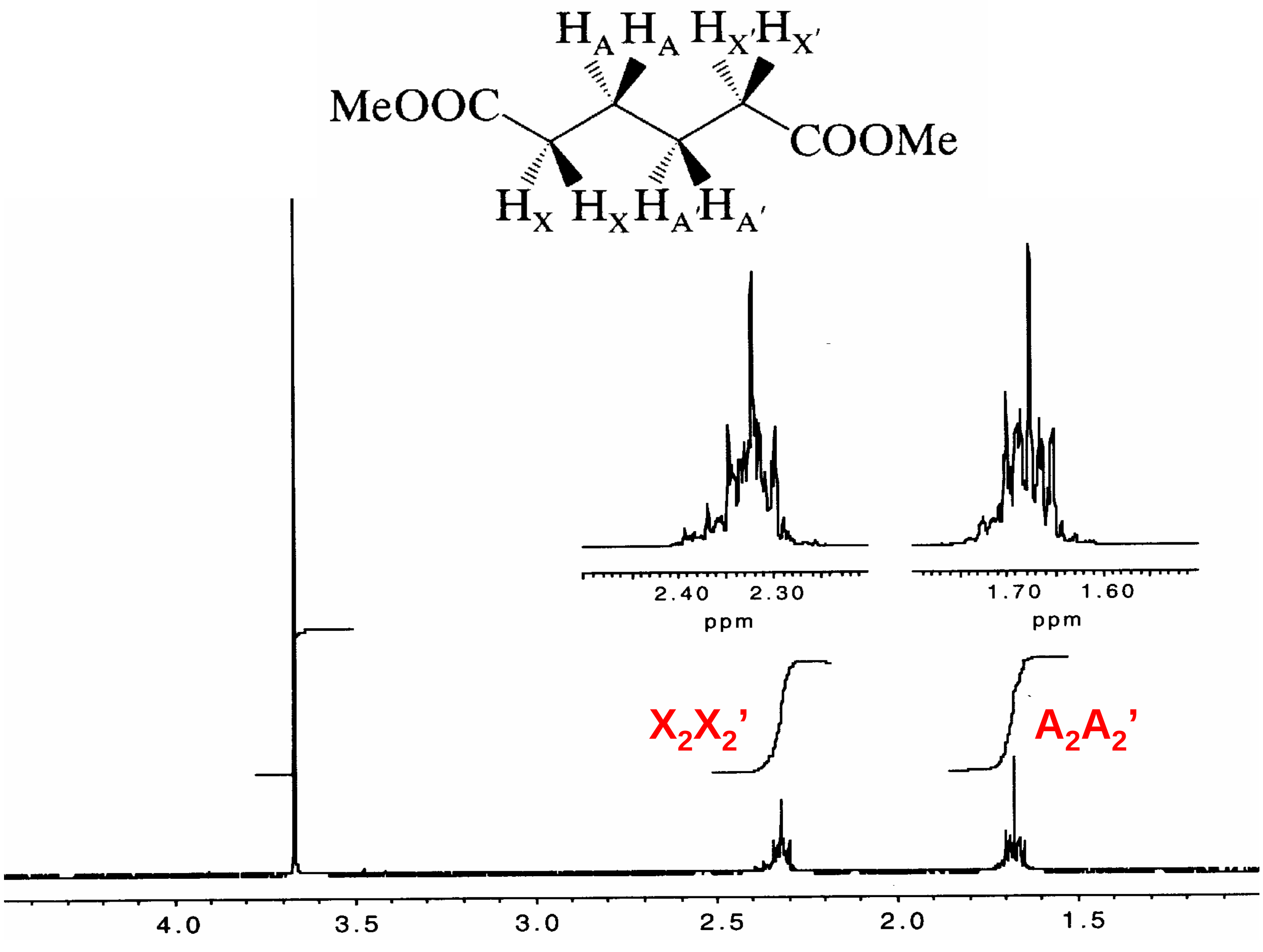
$HOCH_2\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}CH_3$

X_2 A_2 B_2 C_2 D_2 M_3



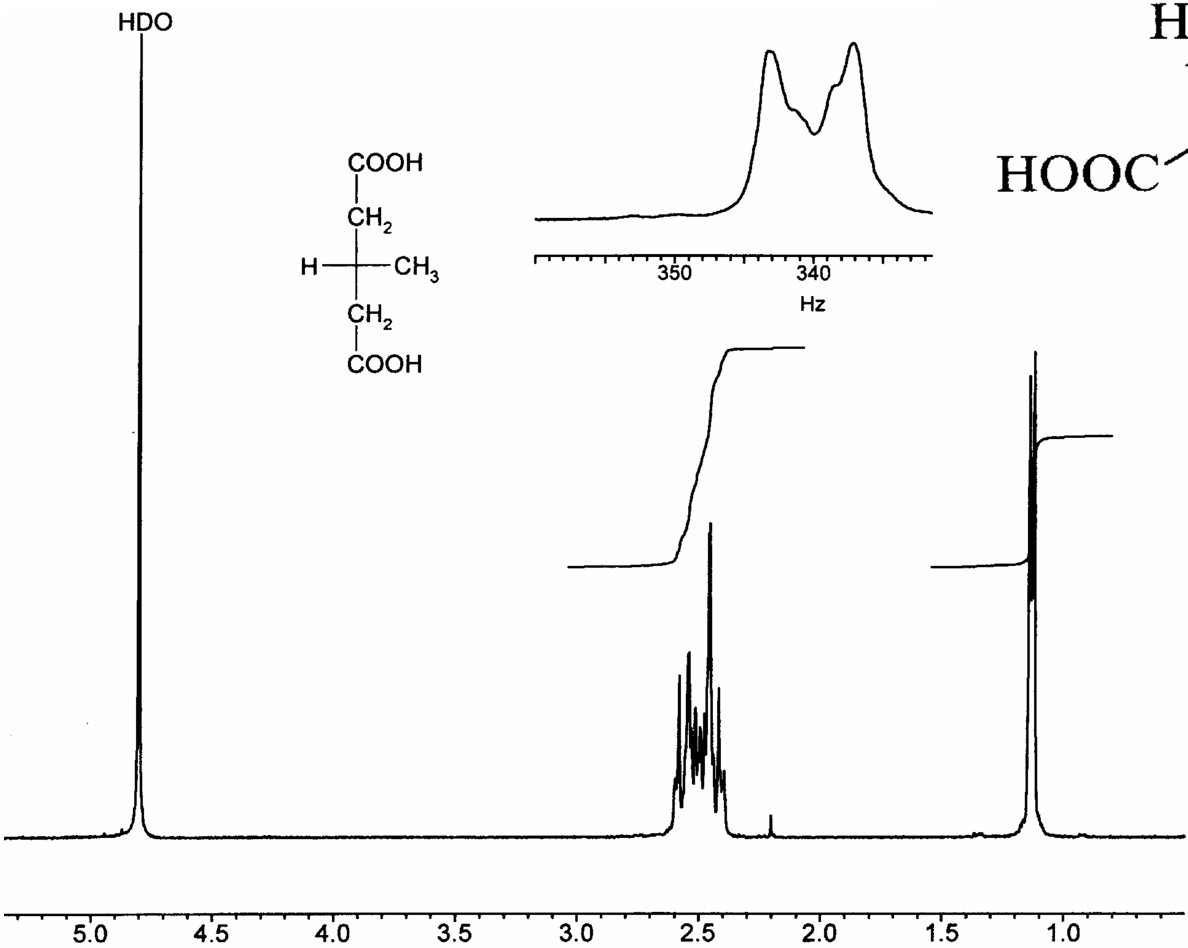
Open-Chain Systems

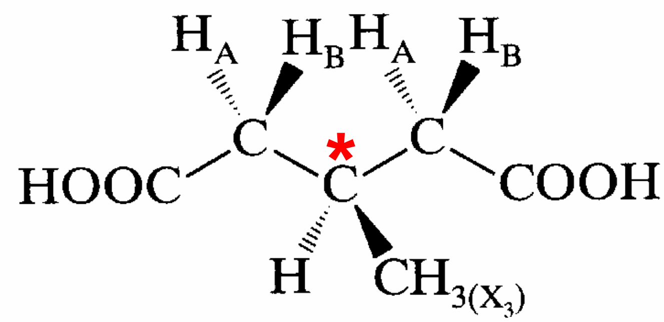
Symmetrical Chains A_2X_2 or (A_2A_2' X_2X_2')



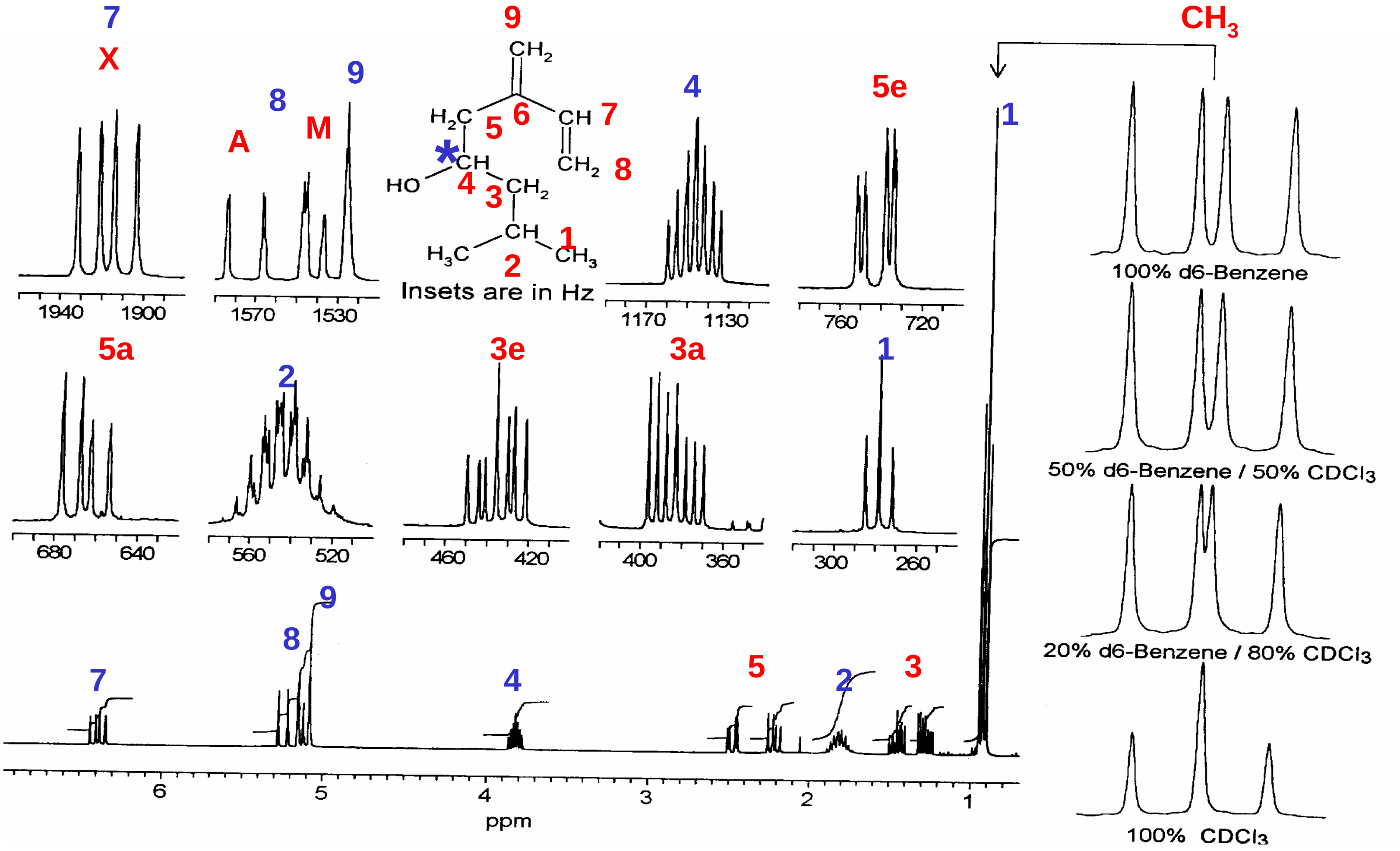
Open-chain systems

Less Symmetrical Chains $A_2B_2MX_3$





Open-chain systems: Less Symmetrical Chains



Chapter 4
^{13}C NMR Spectrometry

^{13}C I = ½ , NMR detectable, but

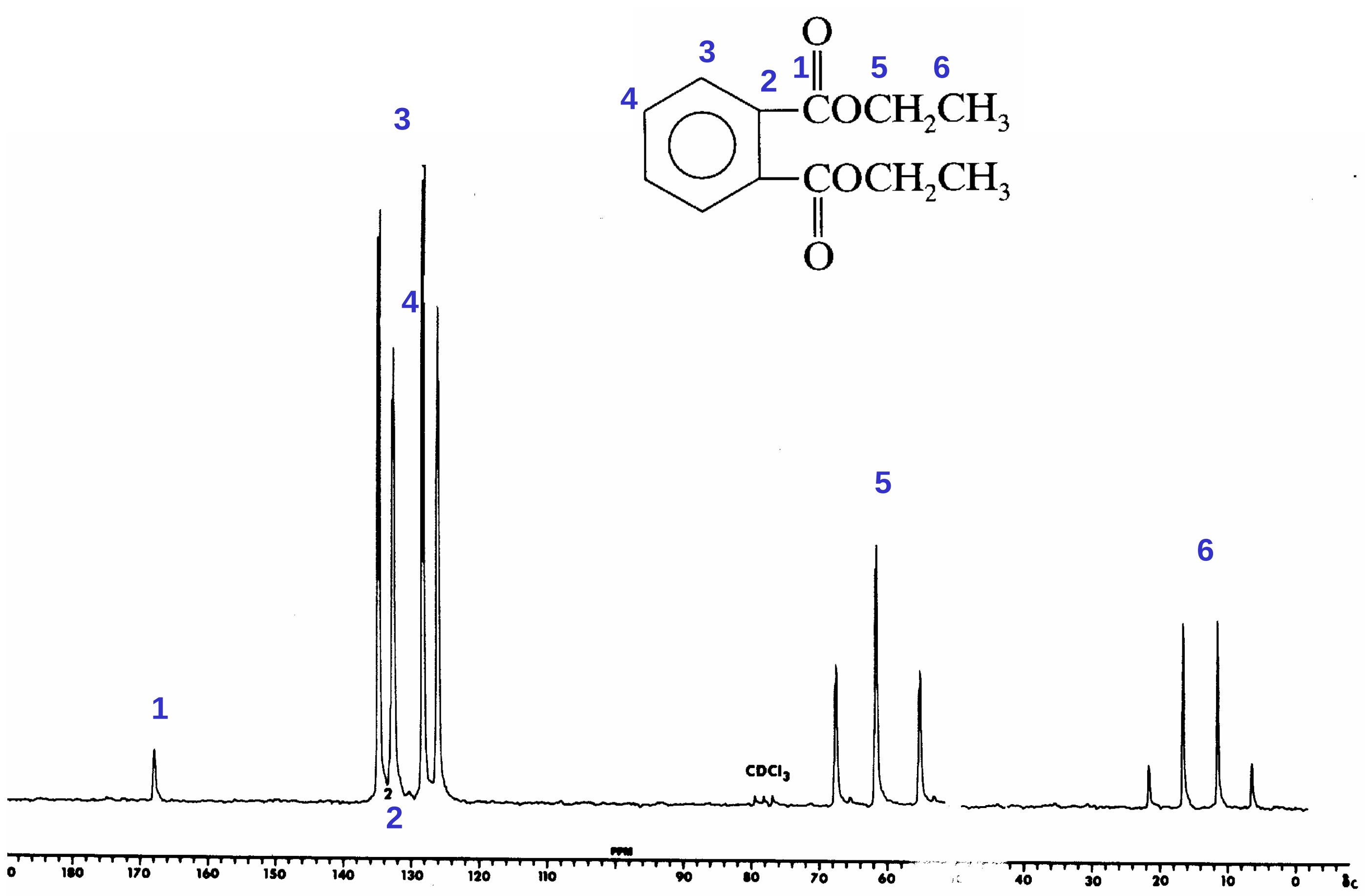
Natural abundance is only1.1 % that of ^{12}C

Sensitivity is only 1.6 % that of ^{1}H

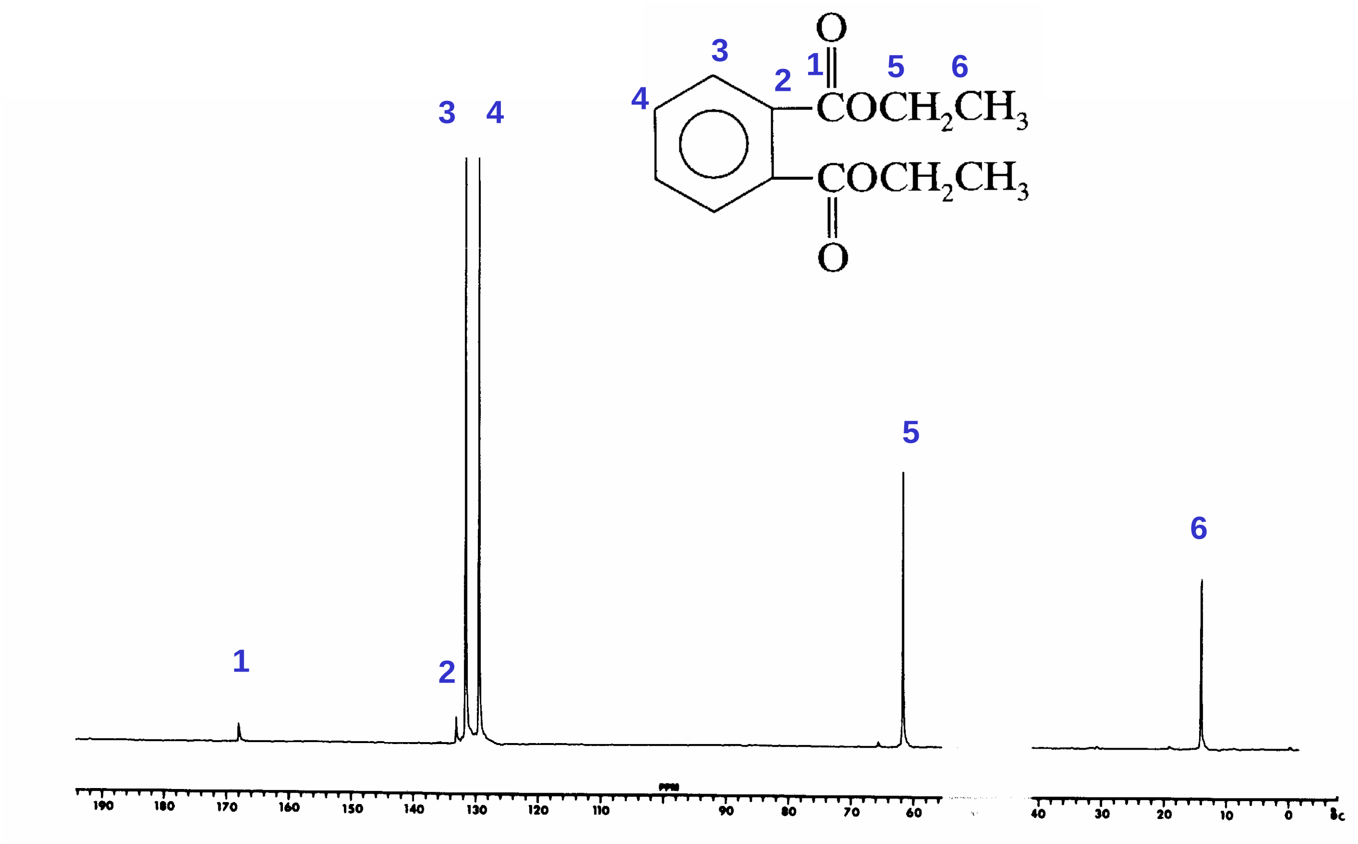
^{12}C I = 0, NMR undetectable

The overall sensitivity of ^{13}C / ^{1}H is 1/5700

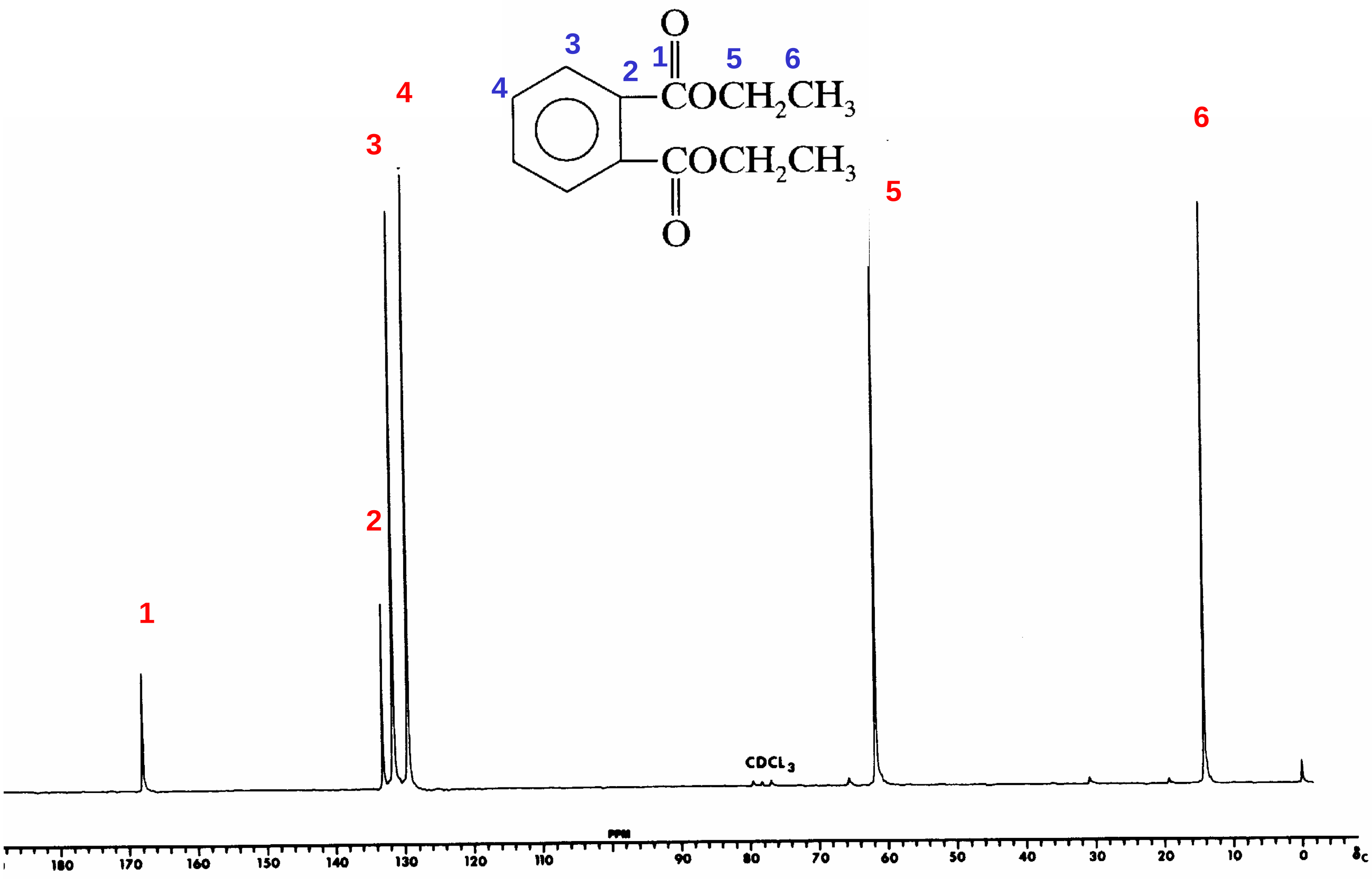
^{13}C NMR Spectrum with Proton-Coupling



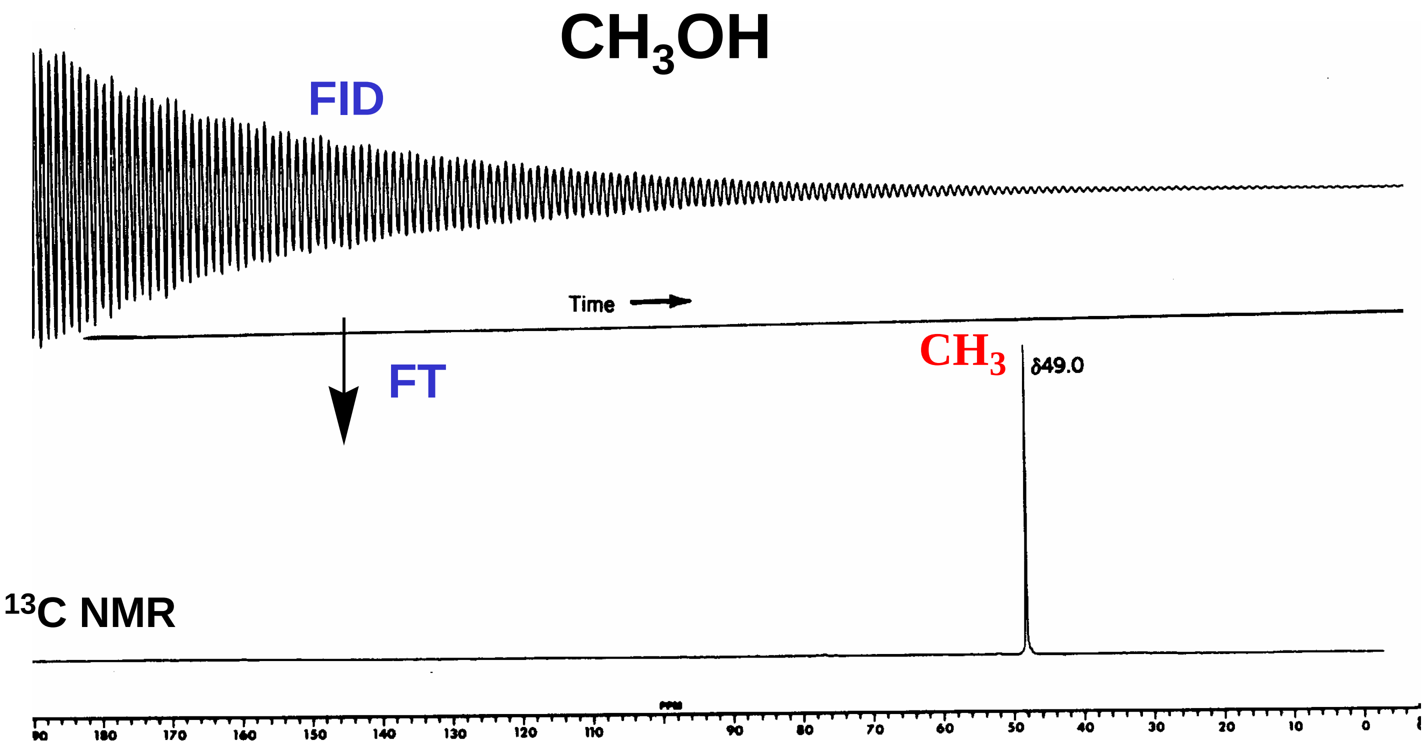
^{13}C NMR Spectrum with Protons Decoupled by the Broadband Decoupler



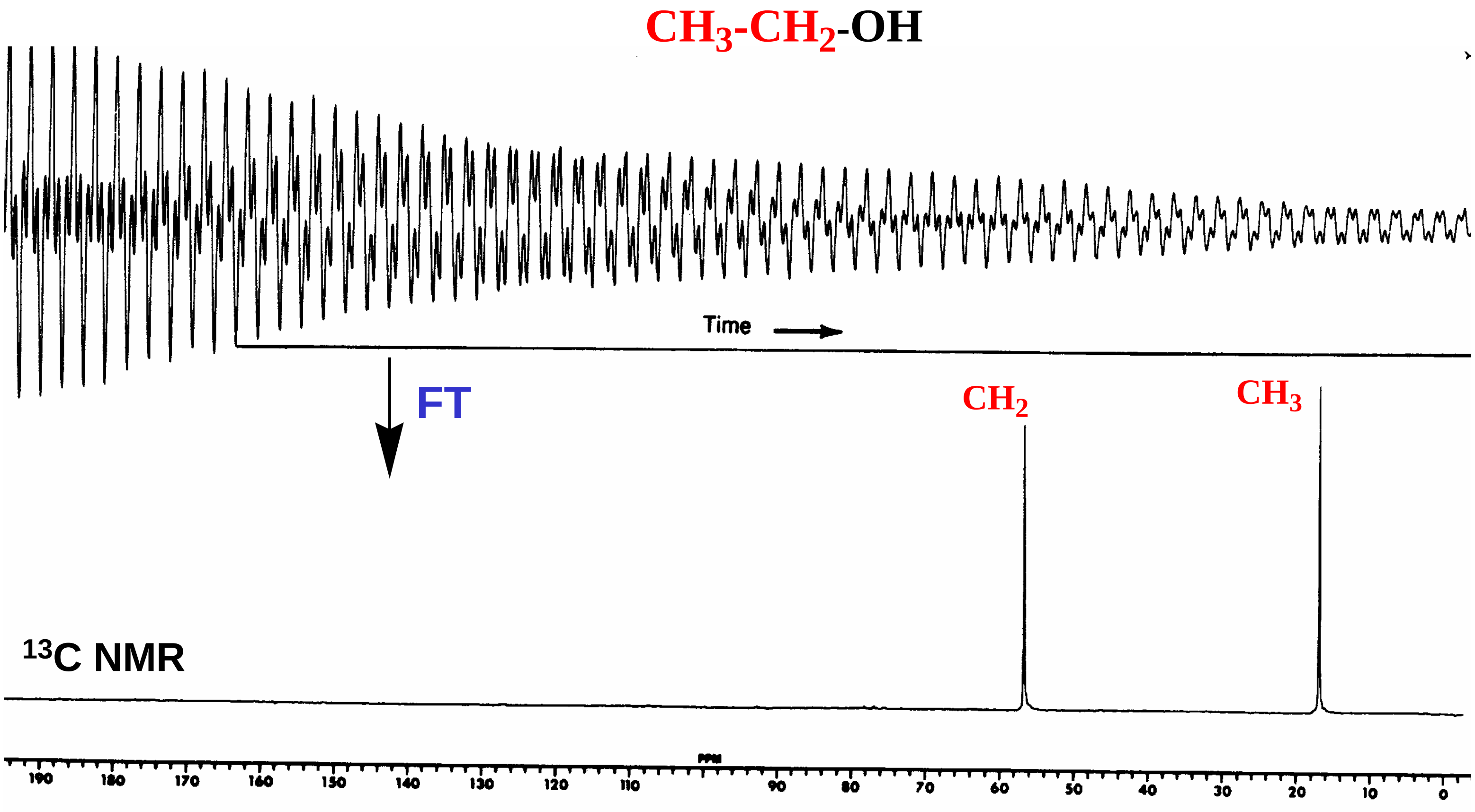
^{13}C NMR Spectrum with Protons Decoupled and a 10-s Delay between Pulses



Free Induction Decay (Time Domain) and Fourier Transformed ^{13}C NMR Spectrum (Frequency Domain), Decoupled

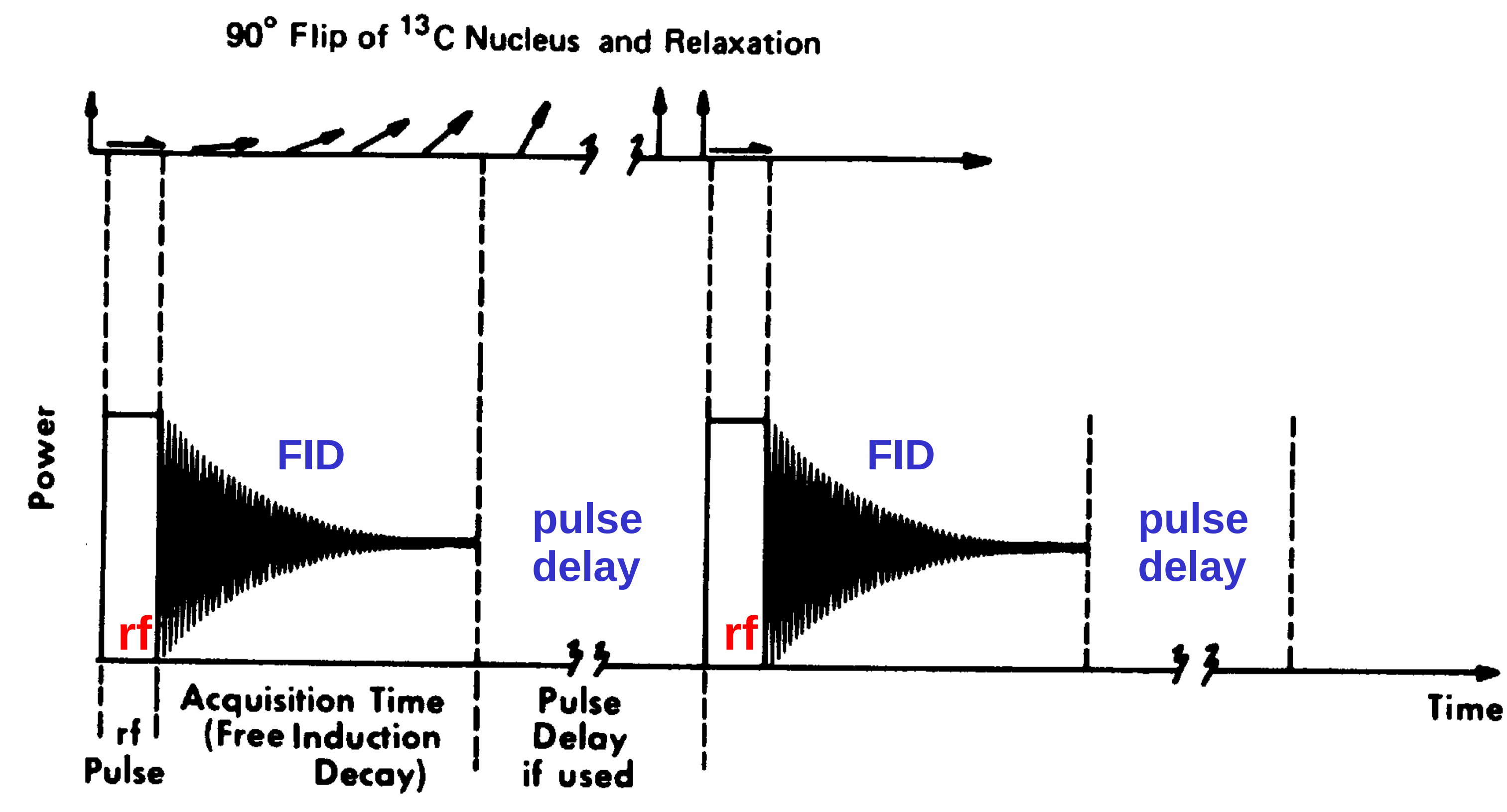


Free Induction Decay (Time Domain) and Fourier Transformed ^{13}C NMR Spectrum (Frequency Domain), Decoupled

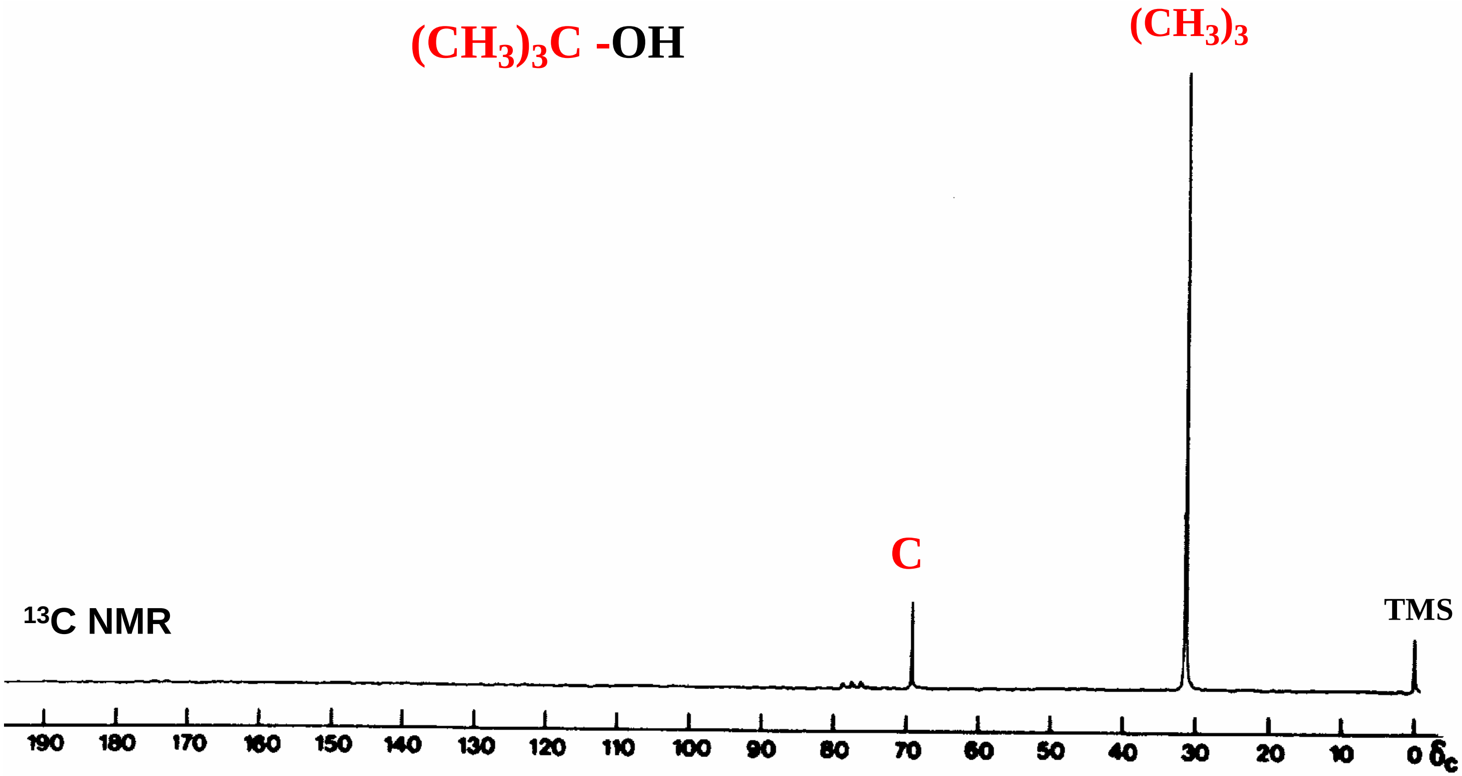


Schematic Representation of

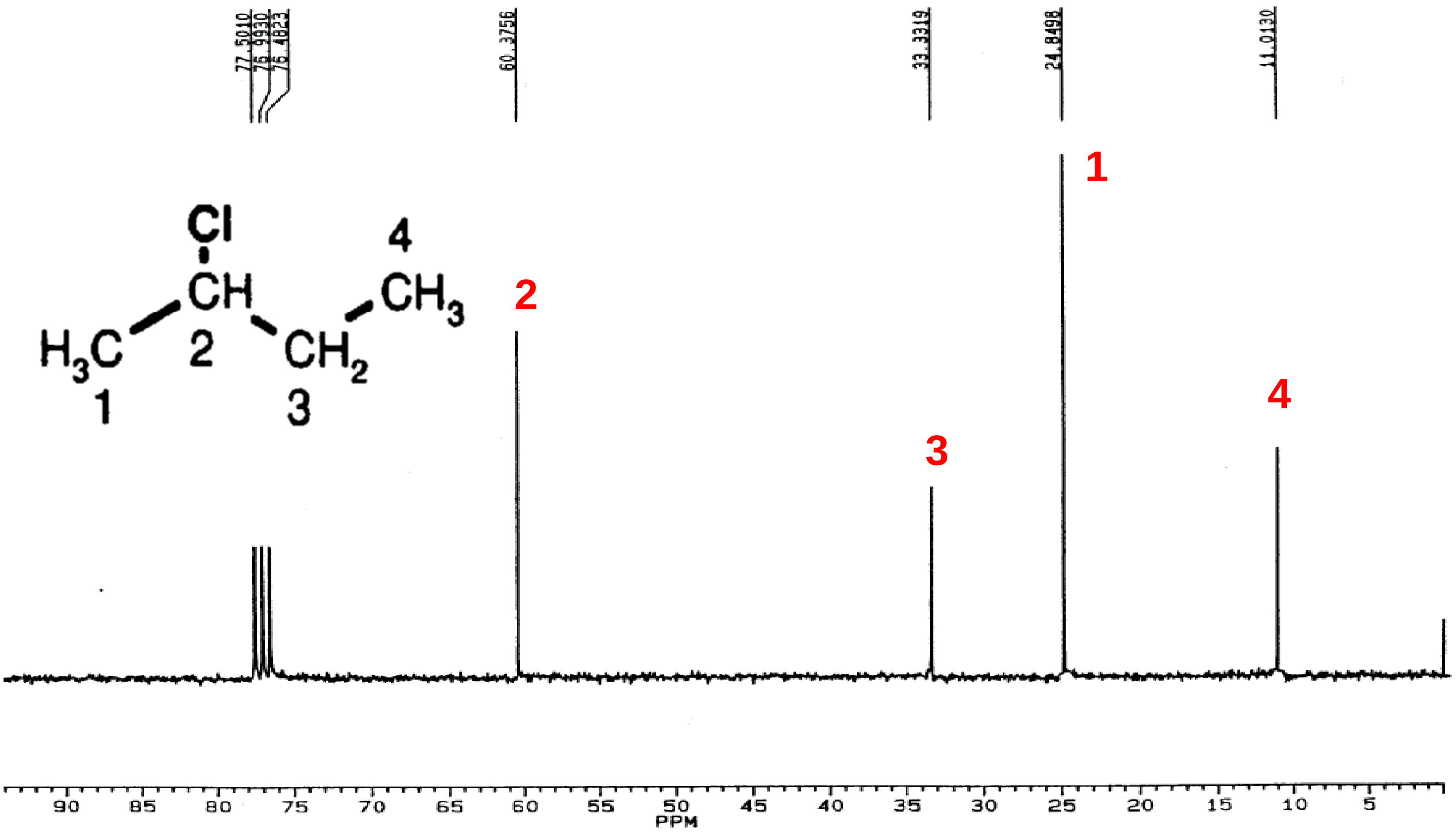
the rf Pulse Followed by the FID and Pulse Delay



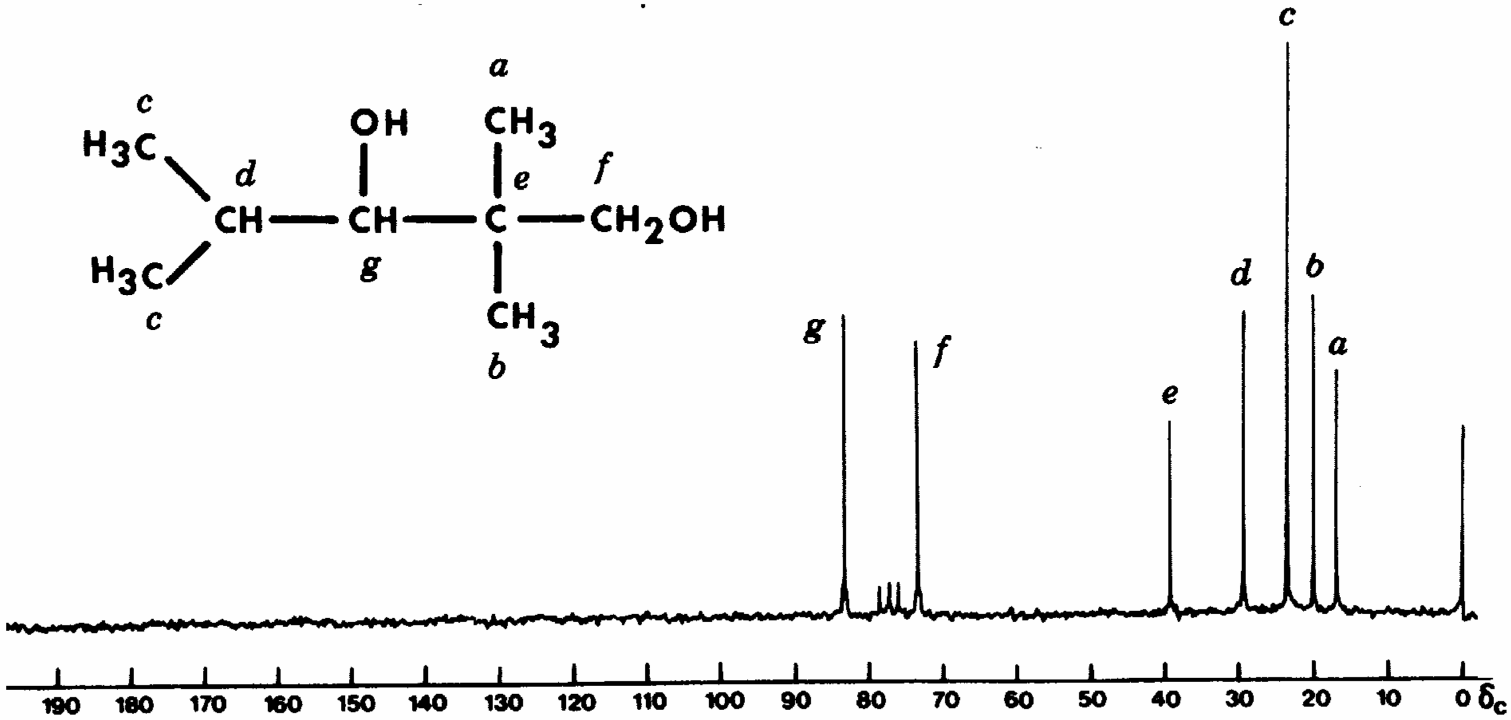
^{13}C NMR with Protons Decoupled by the Broadband Decoupler: An Example



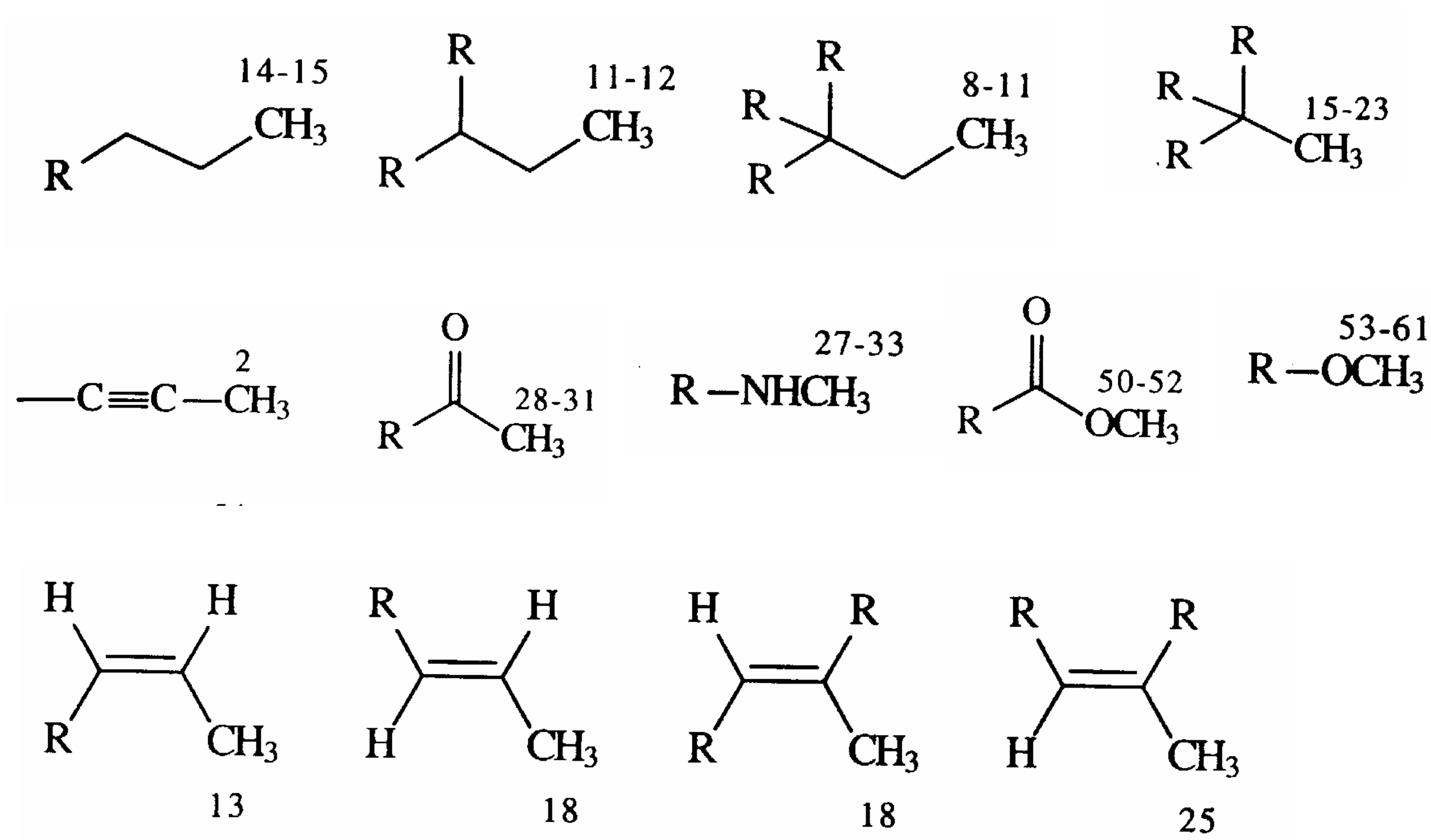
^{13}C NMR with Protons Decoupled by the Broadband Decoupler: An Example



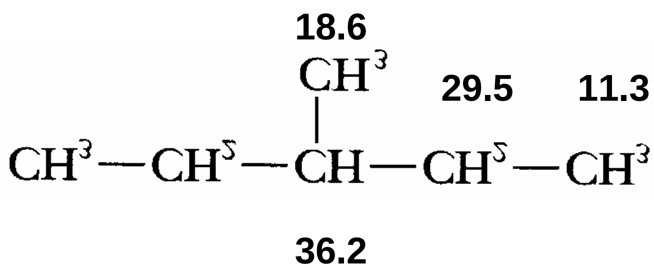
^{13}C NMR with Protons Decoupled by the Broadband Decoupler: An Example

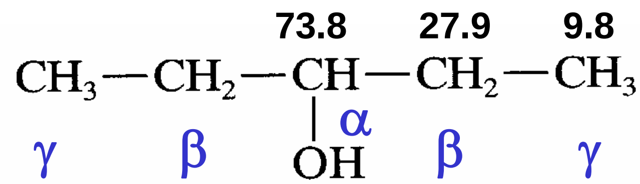


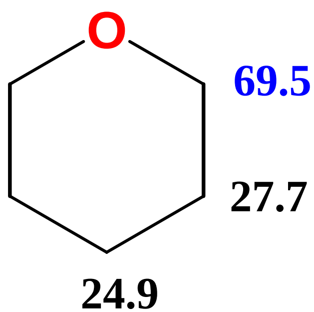
^{13}C NMR Chemical Shifts: Inductive Effect of Substituents on Alkanes

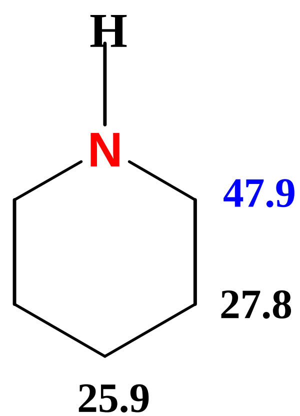


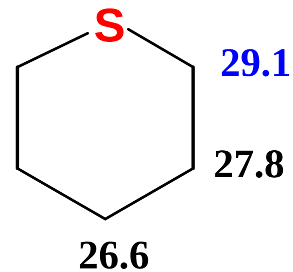
^{13}C NMR Chemical Shifts: Inductive Effect of Substituents on Alkanes and Cycloalkanes

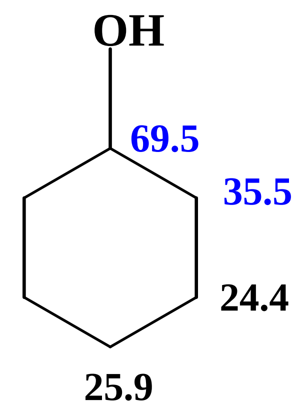






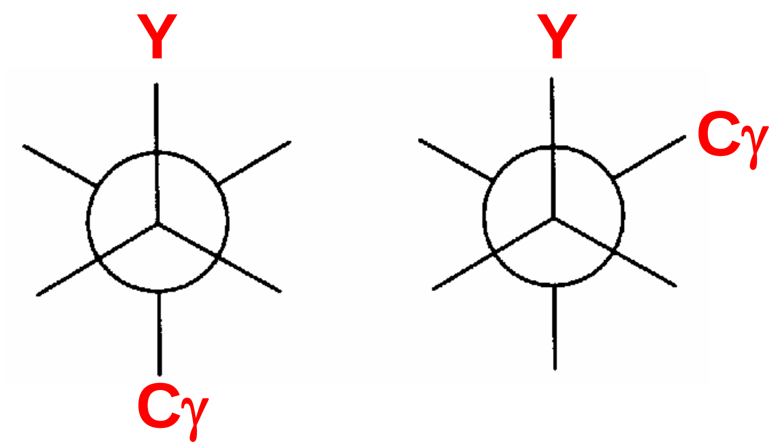






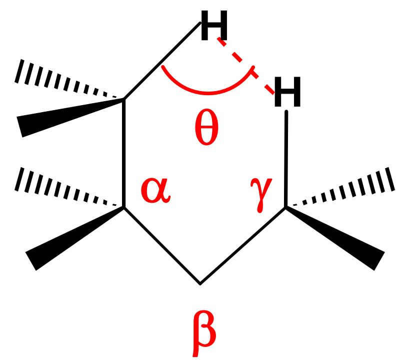
^{13}C NMR Chemical Shifts: γ Gauche Interaction on Alkanes

γ gauche interaction



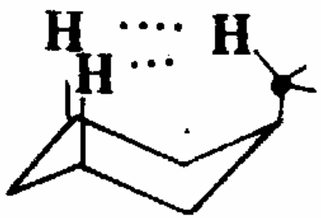
Y = N, O, F

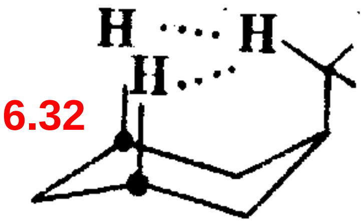
anti gauche

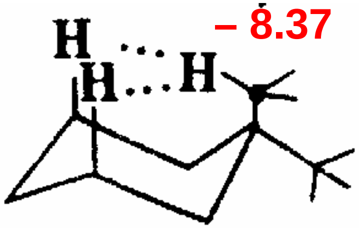


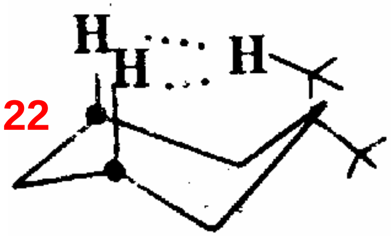
$$\Delta \delta_{st} = C\, F_{HH}\, (\gamma_{HH}) \cos \theta$$

^{13}C NMR Chemical Shifts: γ Gauche Interaction on Cycloalkanes

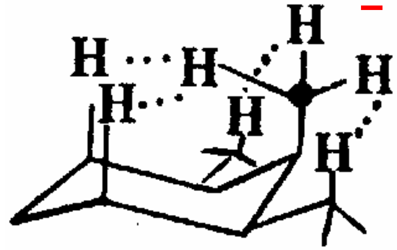




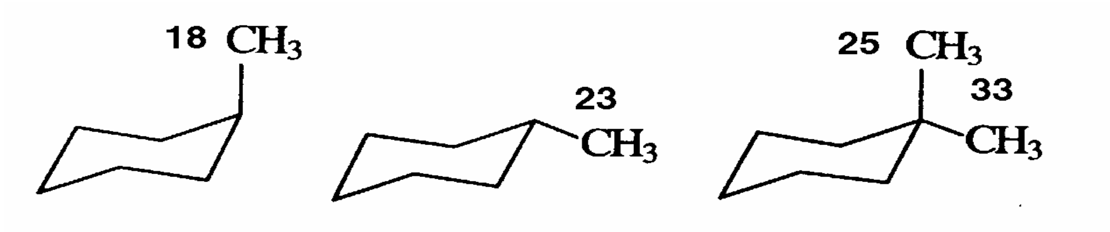


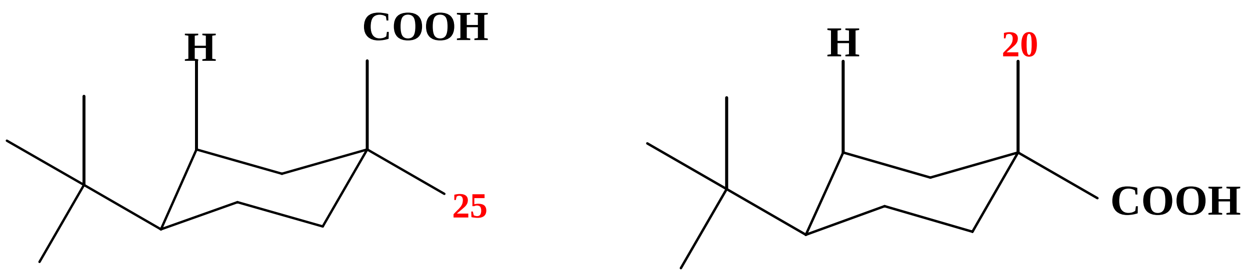






^{13}C NMR Chemical Shifts: γ Gauche Interaction on Cycloalkanes

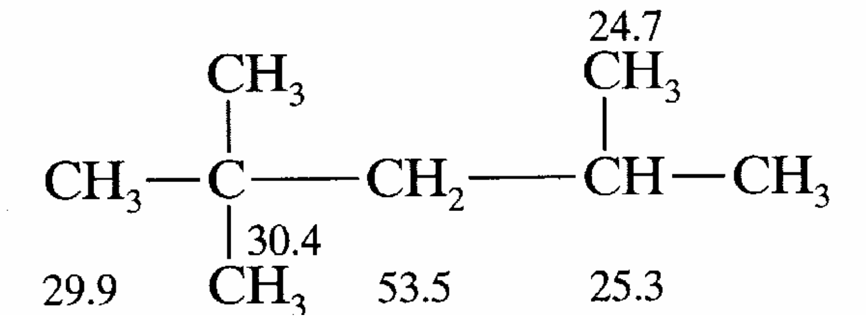


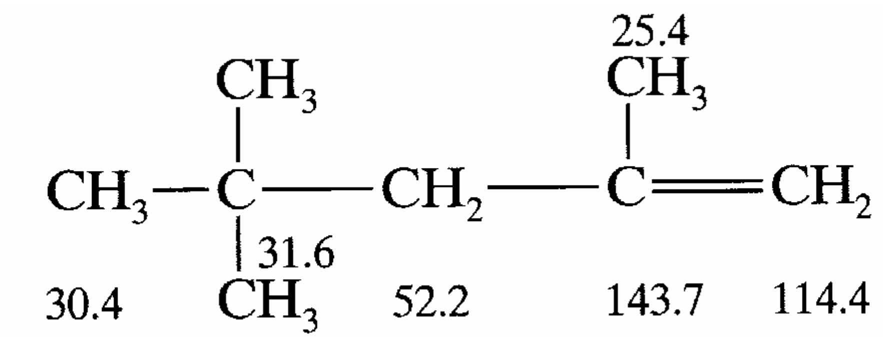


^{13}C NMR Chemical Shifts: Effects of Substituents on Alkenes

$H_2C{=}CH_2$

123.2

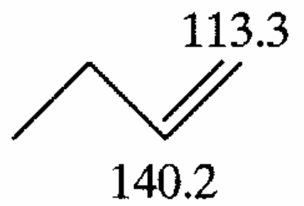


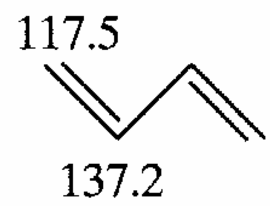


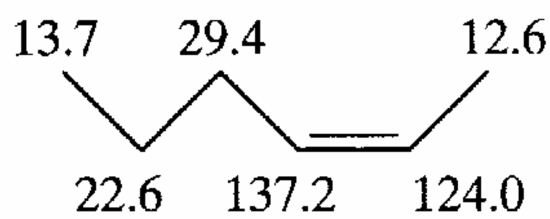
^{13}C NMR Chemical Shifts: Conjugative Effects of Substituents on Alkenes

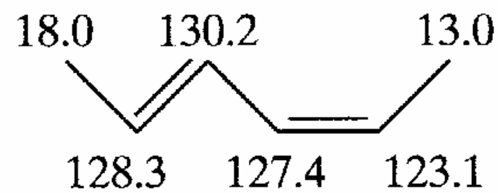
$H_2C=CH_2$

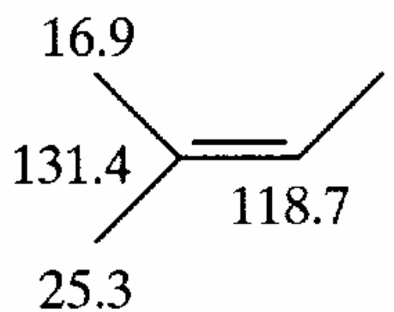
123.2

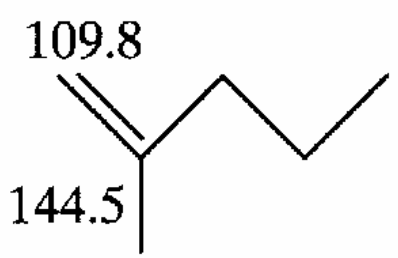




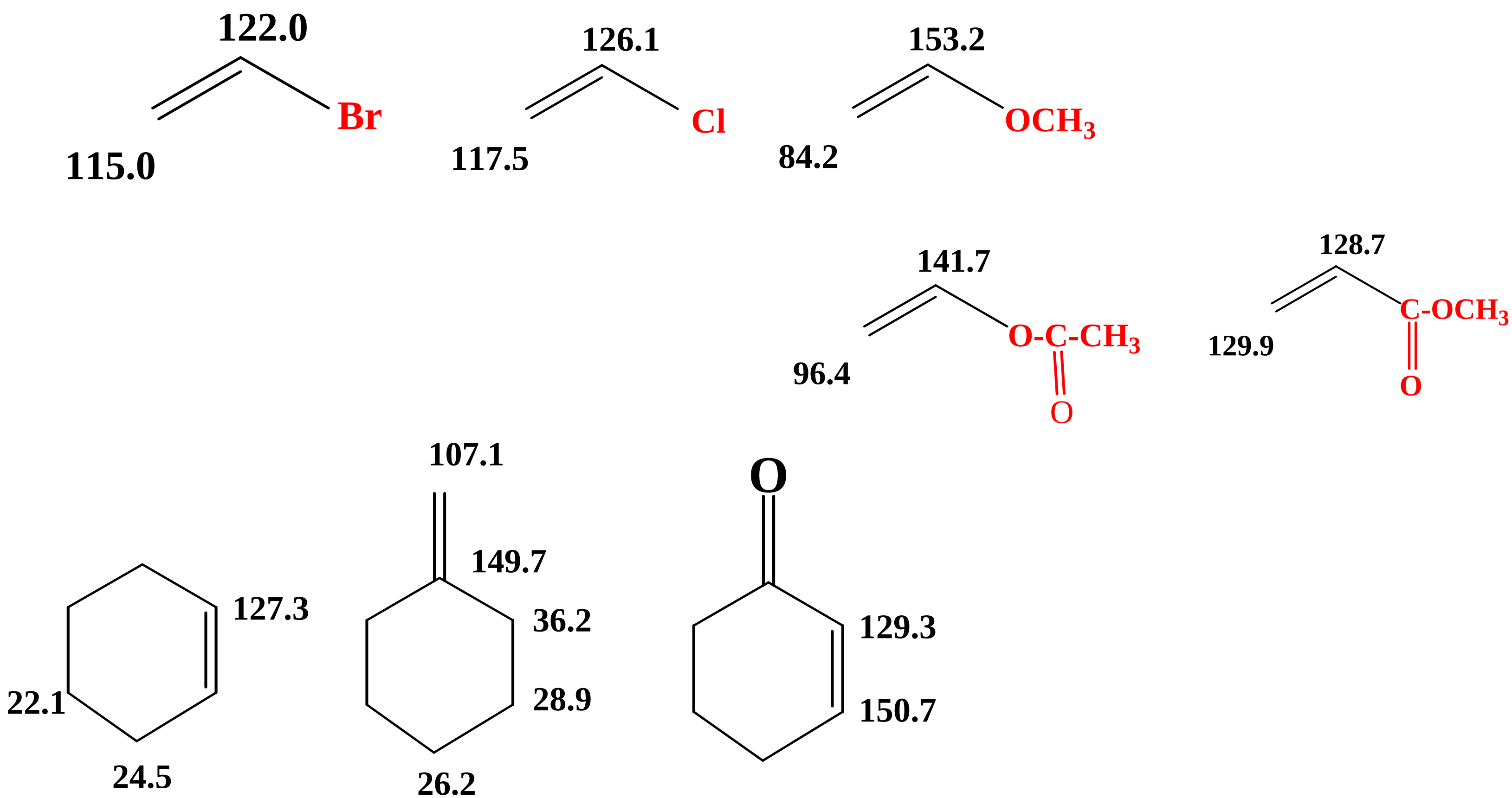




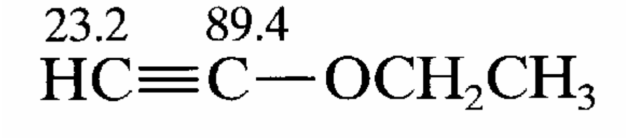


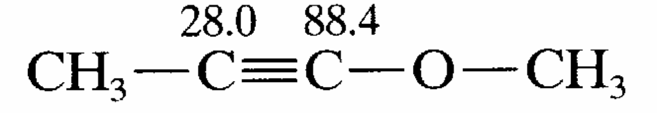


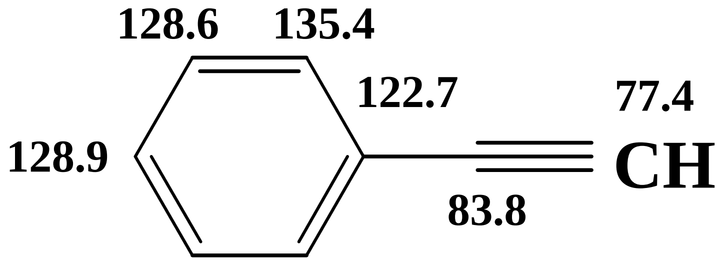
^{13}C NMR Chemical Shifts: Inductive Effects of Substituents on Alkenes and Cycloalkenes



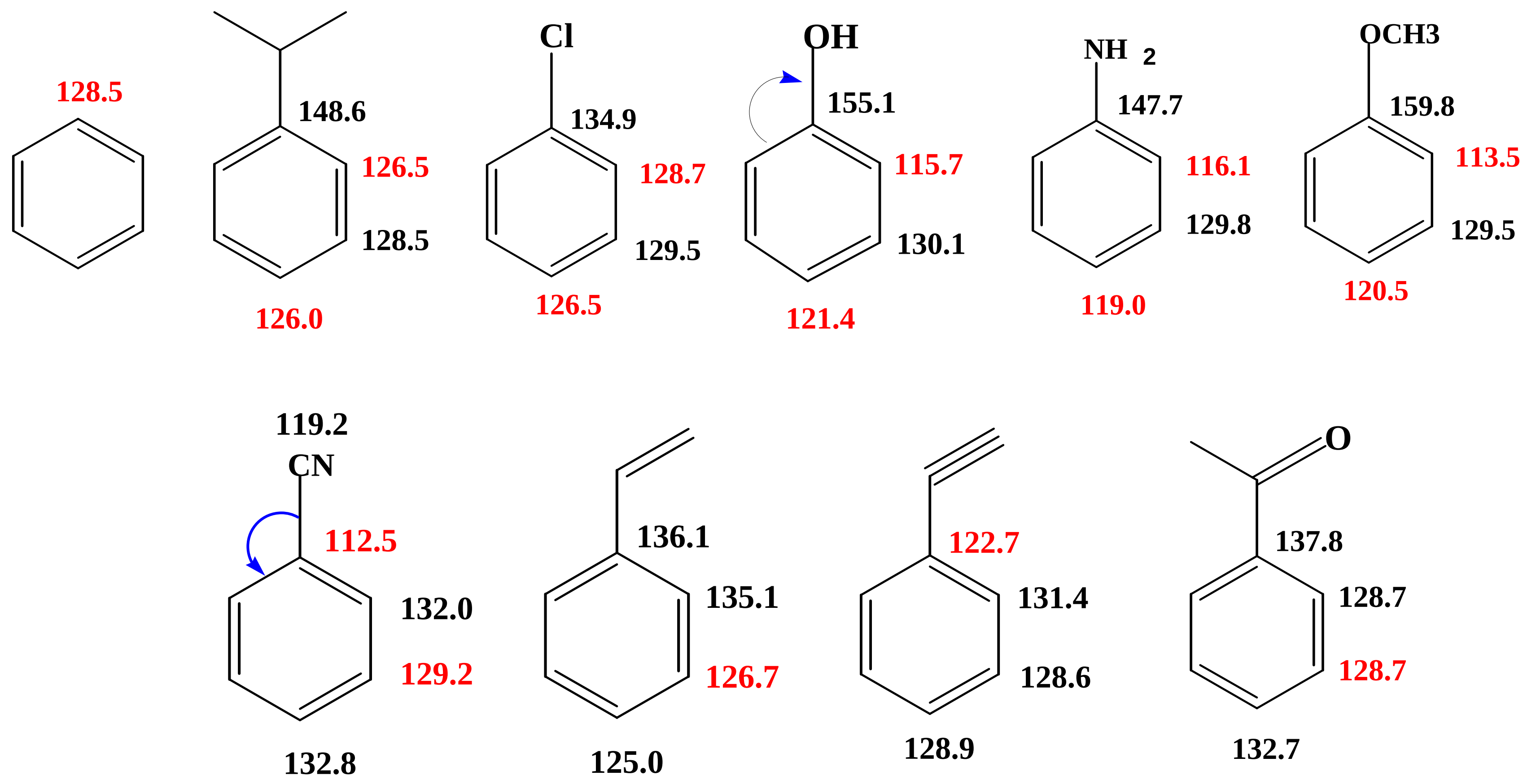
^{13}C NMR Chemical Shifts: Effect of Substituents on Alkynes



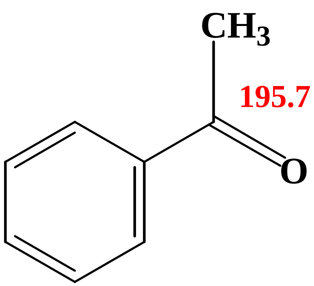




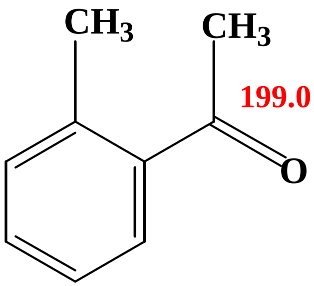
^{13}C NMR Chemical Shifts: Inductive and Conjugative Effects of Substituents on Aromatic Compounds



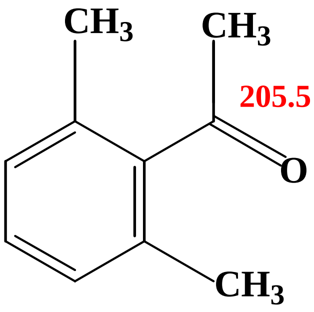
^{13}C NMR Chemical Shifts: Conjugative Effects of Substituents on Aromatic Compounds



$\theta = 0^{o}$

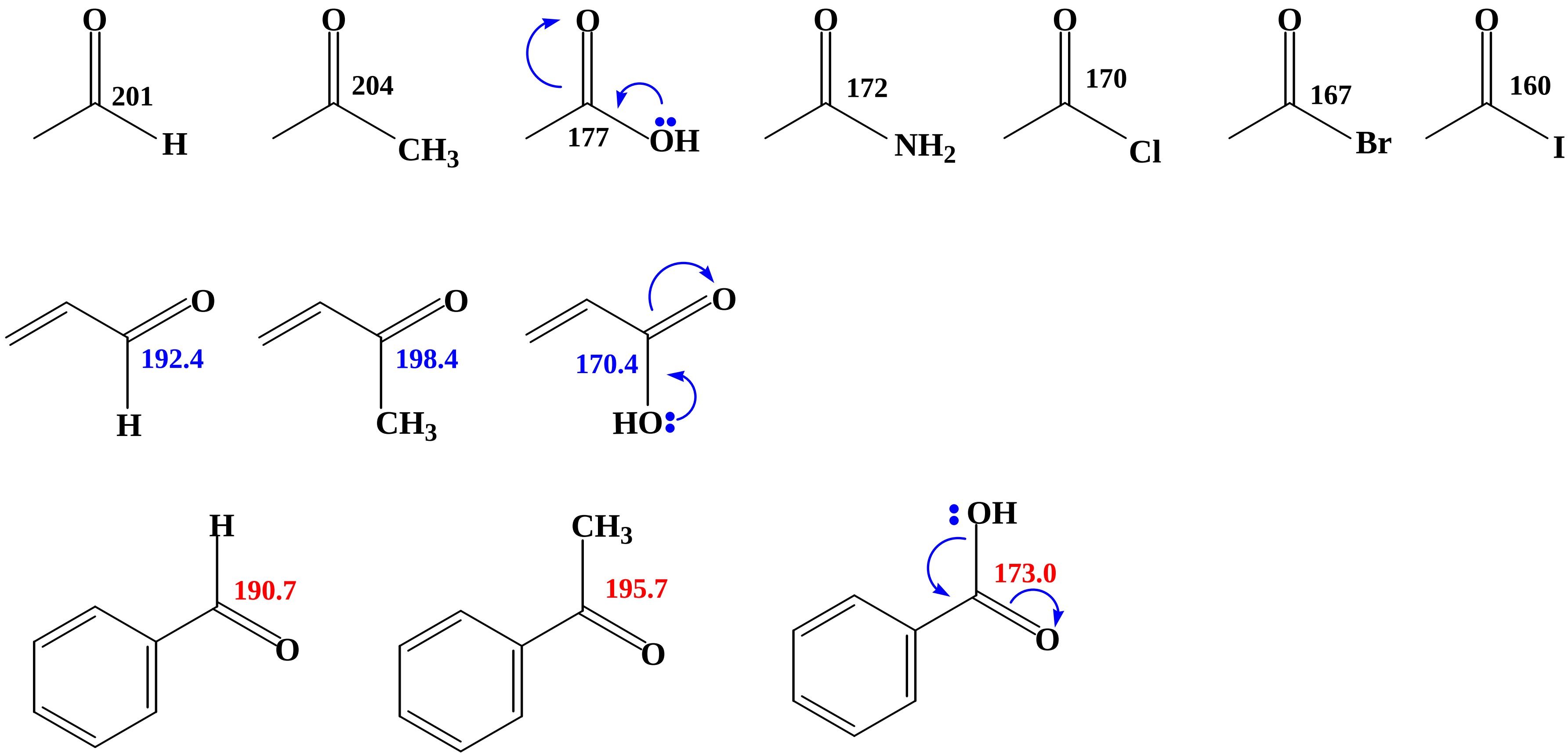


$\theta = 28^{o}$

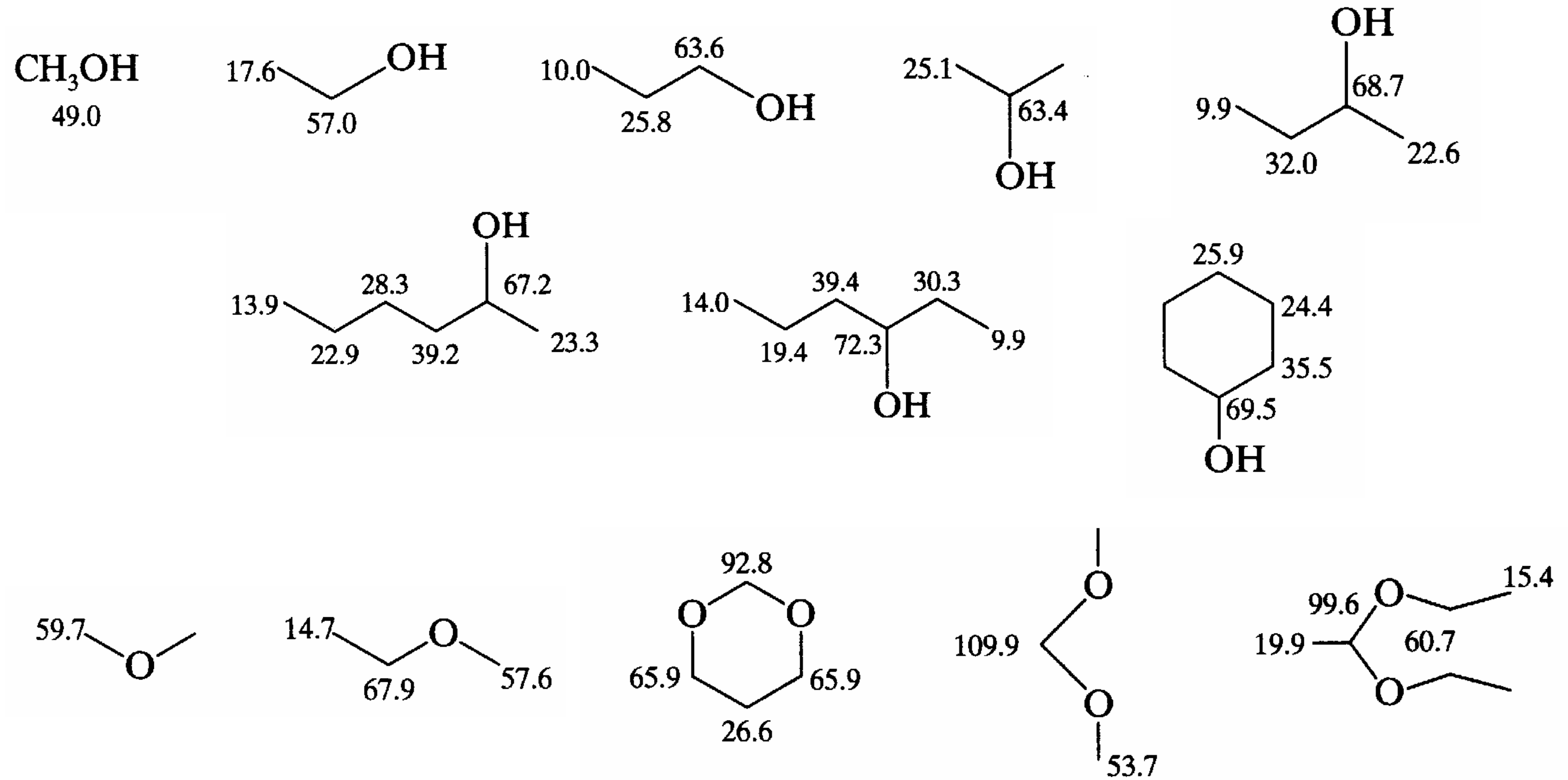


$\theta = 50^{o}$

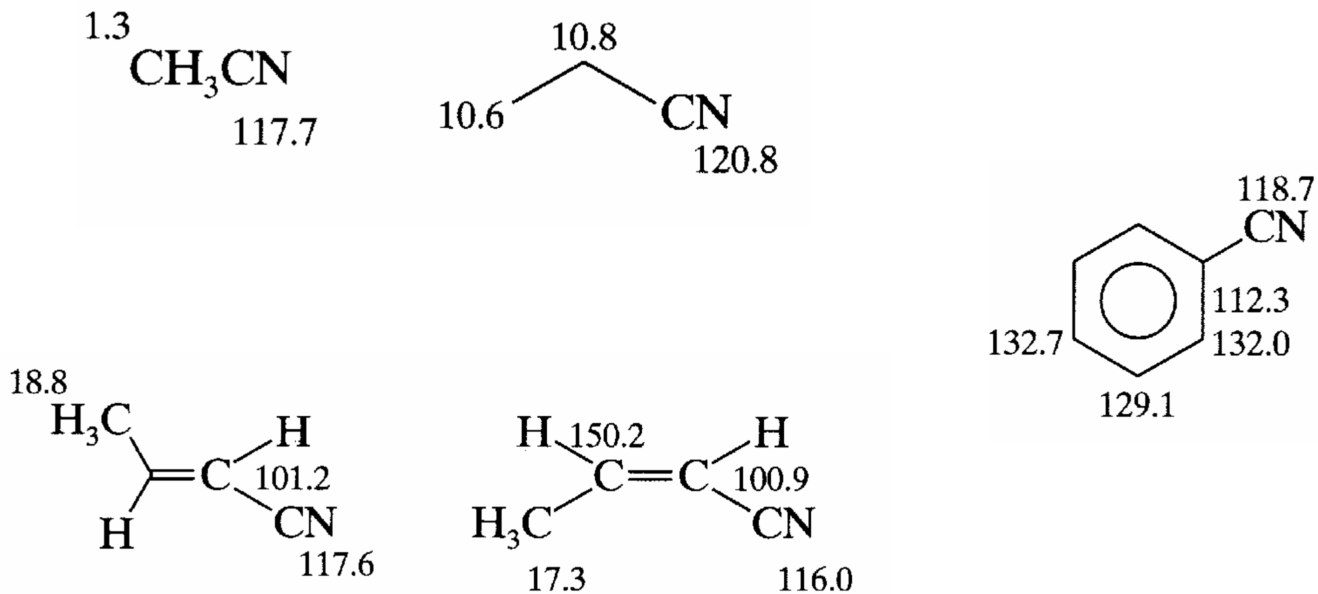
^{13}C NMR Chemical Shifts of Carbonyl Groups



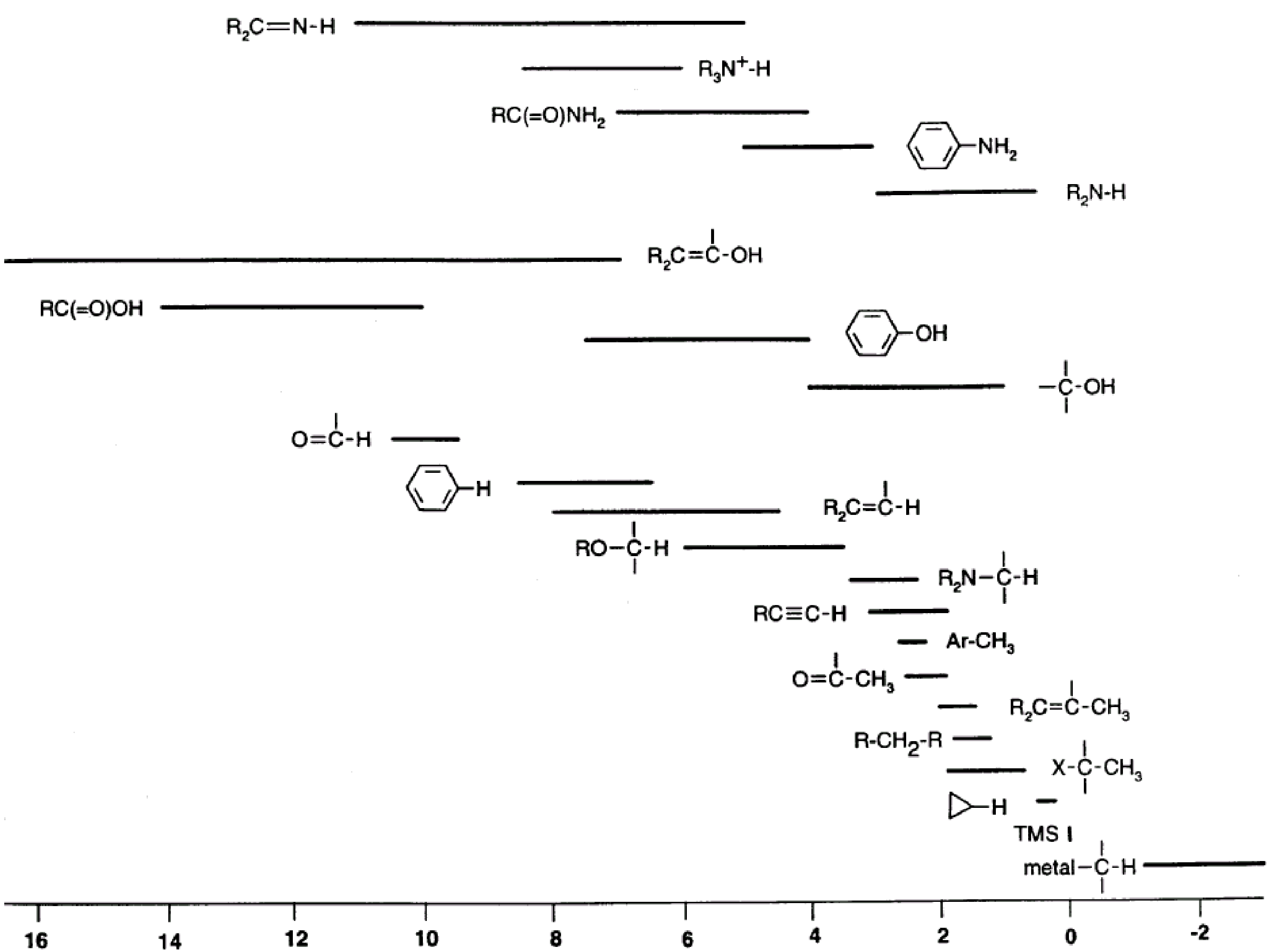
^{13}C NMR Chemical Shifts of Alcohols and Ethers



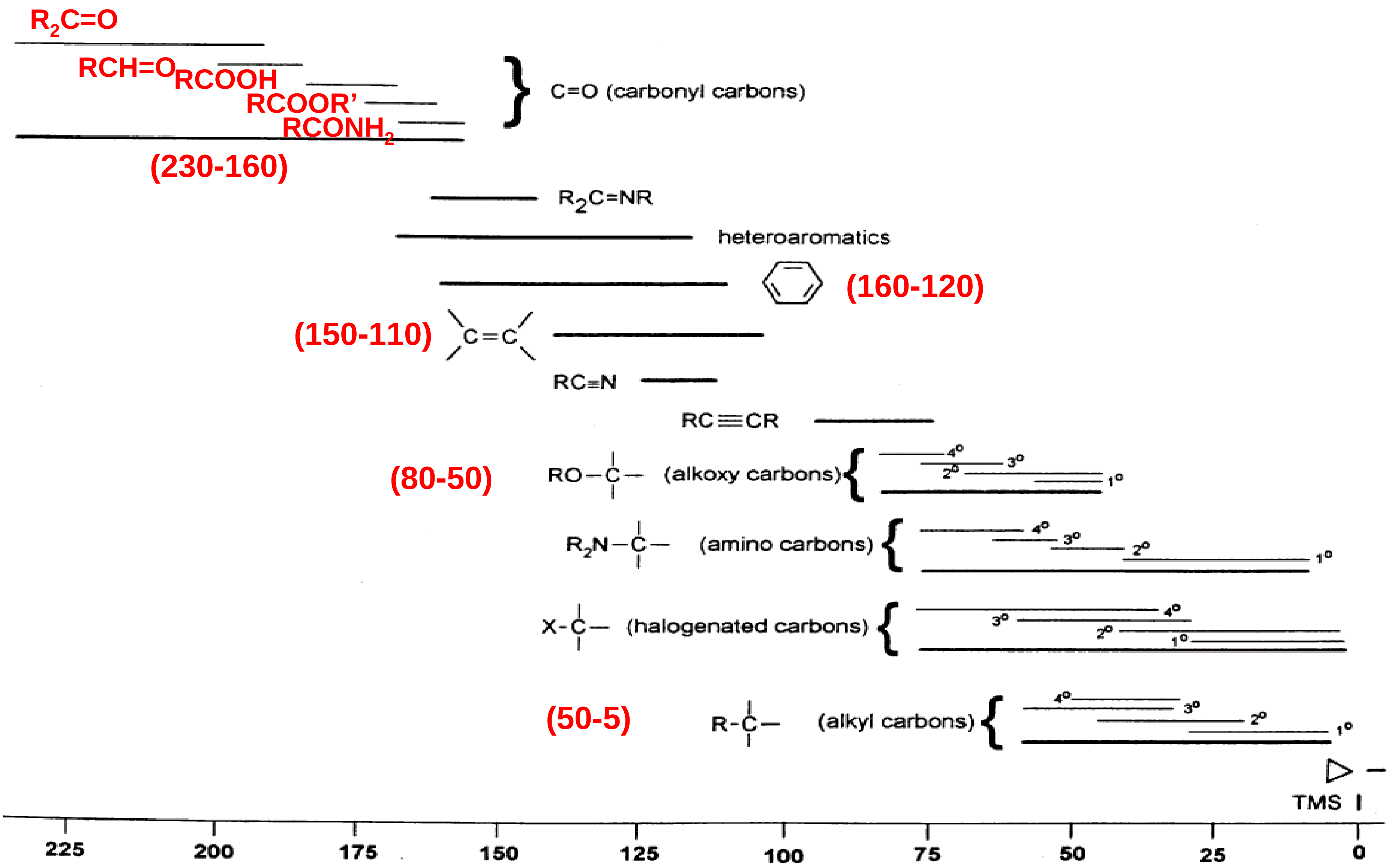
^{13}C NMR Chemical Shifts of Nitriles



^{1}H Chemical Shifts of Common Structures



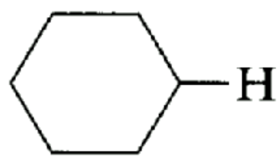
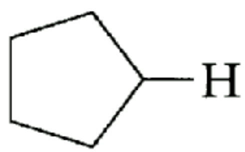
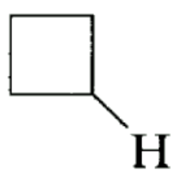
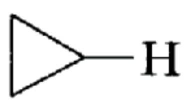
^{13}C Chemical Shifts of Common Structures



^{13}C-^{1}H Spin Coupling: Some $^{1}J_{CH}$ values

Compound	$^{1}J_{CH}$ J (Hz)
sp^3	
CH_3CH_3	124.9
$CH_3\underline{C}H_2CH_3$	119.2
$(CH_3)_3CH$	114.2
CH_3NH_2	133.0
CH_3OH	141.0
CH_3Cl	150.0
CH_2Cl_2	178.0
$CHCl_3$	209.0

^{13}C-^{1}H Spin Coupling: Some $^{1}J_{CH}$ values

Compound	J (Hz)
sp^3	
	123.0
	128.0
	134.0
	161.0

^{13}C-^{1}H Spin Coupling: Some $^{1}J_{CH}$ values

Compound	$^{1}J_{CH}$ J (Hz)
sp^2	
$CH_2{=}CH_2$	156.2
$CH_3\underline{C}H{=}C(CH_3)_2$	148.4
$CH_3\underline{C}H{=}O$	172.4
$NH_2\underline{C}H{=}O$	188.3
C_6H_6	159.0

^{13}C-^{1}H Spin Coupling: Some $^{1}J_{CH}$ values

Compound	$^{1}J_{CH}$ *J* (Hz)
sp	
CH≡CH	249.0
C_6H_5C≡CH	251.0
HC≡N	269.0

^{13}C-^{1}H Spin Coupling: Some $^{2}J_{CH}$ values

Compound	$^{2}J_{CH}$ *J* (Hz)
sp^3	
$C\underline{H}_3\underline{C}H_3$	−4.5
$C\underline{H}_3\underline{C}Cl_3$	5.9
$\underline{C}H_3C\underline{H}{=}O$	26.7

^{13}C-^{1}H Spin Coupling: Some $^{2}J_{CH}$ values

Compound	$^{2}J_{CH}$ J (Hz)
sp^{2}	
$CH_2{=}CH_2$	−2.4
$(CH_3)_2C{=}O$	5.5
$CH_2{=}CHCH{=}O$	26.9
*C_6H_6	1.0

* $^{3}J = 7.6\ (>{}^{2}J)$

^{13}C-^{1}H Spin Coupling: Some $^{2}J_{CH}$ values

Compound	$^{2}J_{CH}$ *J* (Hz)
sp	
CH≡CH (H and C underlined)	49.3
$C_6H_5OC \equiv CH$ (C and H underlined)	61.0

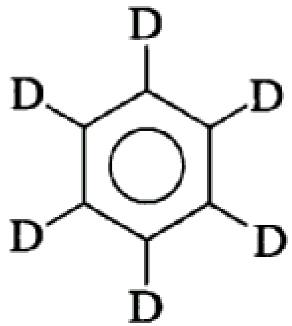
Coupling Constants for ^{19}F Coupled to ^{13}C

Compound	$^{1}J_{CF}$ ^{1}J (Hz)	$^{2}J_{CF}$ ^{2}J (Hz)
CH_3CF_3	271	
CF_2H_2	235	
CF_3CO_2H	284	43.7
C_6H_5F	245	21.0

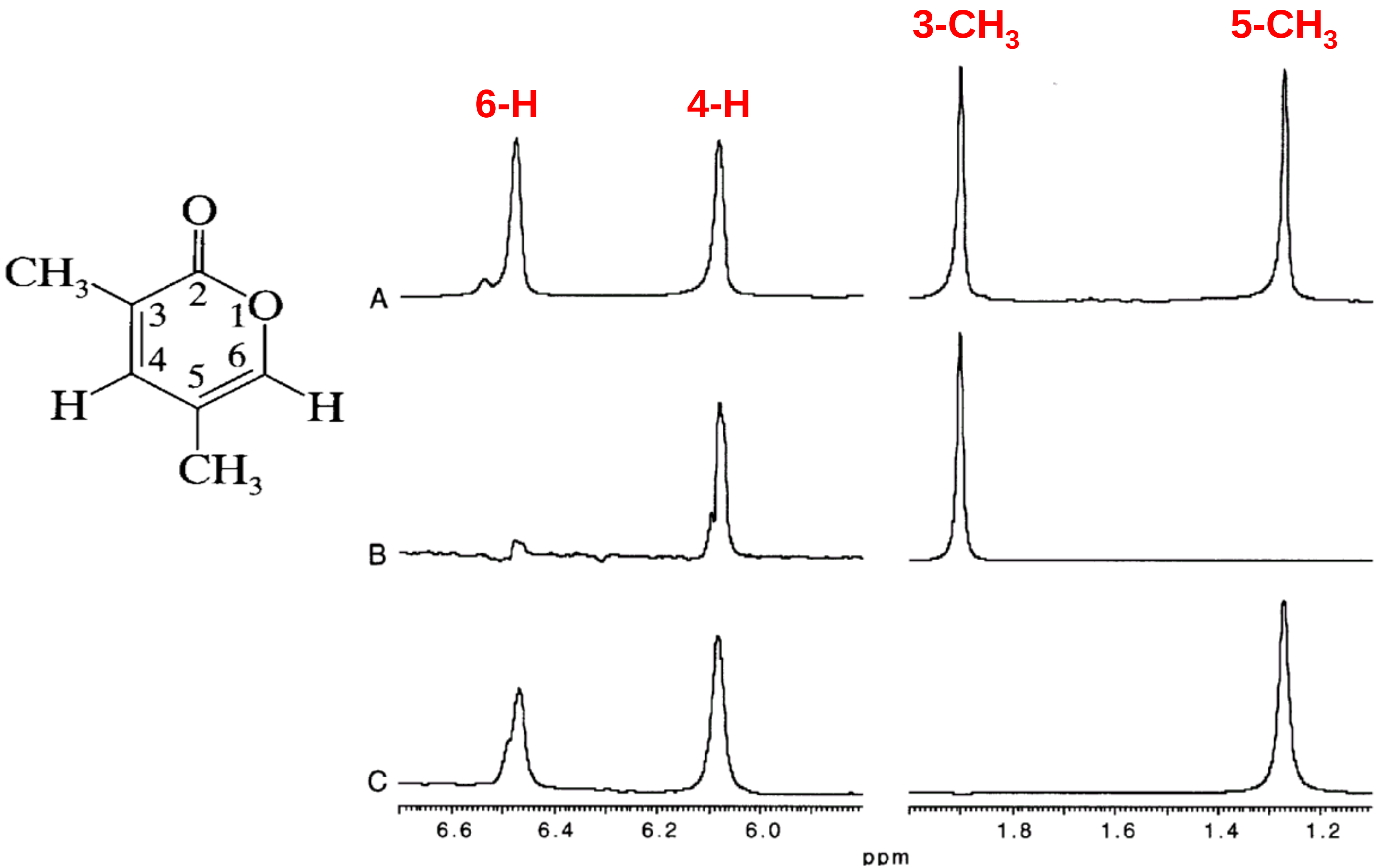
Coupling Constants for ^{31}P Coupled to ^{13}C

Compound	$^1J_{CP}$ ^1J (Hz)	$^2J_{CP}$ ^2J (Hz)	$^3J_{CP}$ ^3J (Hz)
$(CH_3CH_2)_4P^+ Br^-$	49	4.3	
$(C_6H_5)_3P^+CH_3 I^-$	88 (CH_3 52)	10.9	
$CH_3CH_2P(=O)(OCH_2CH_3)_2$	143	7.1 (J_{COP} 6.9)	J_{CCOP} 6.2
$(C_6H_5)_3P$	12.4	19.6	6.7

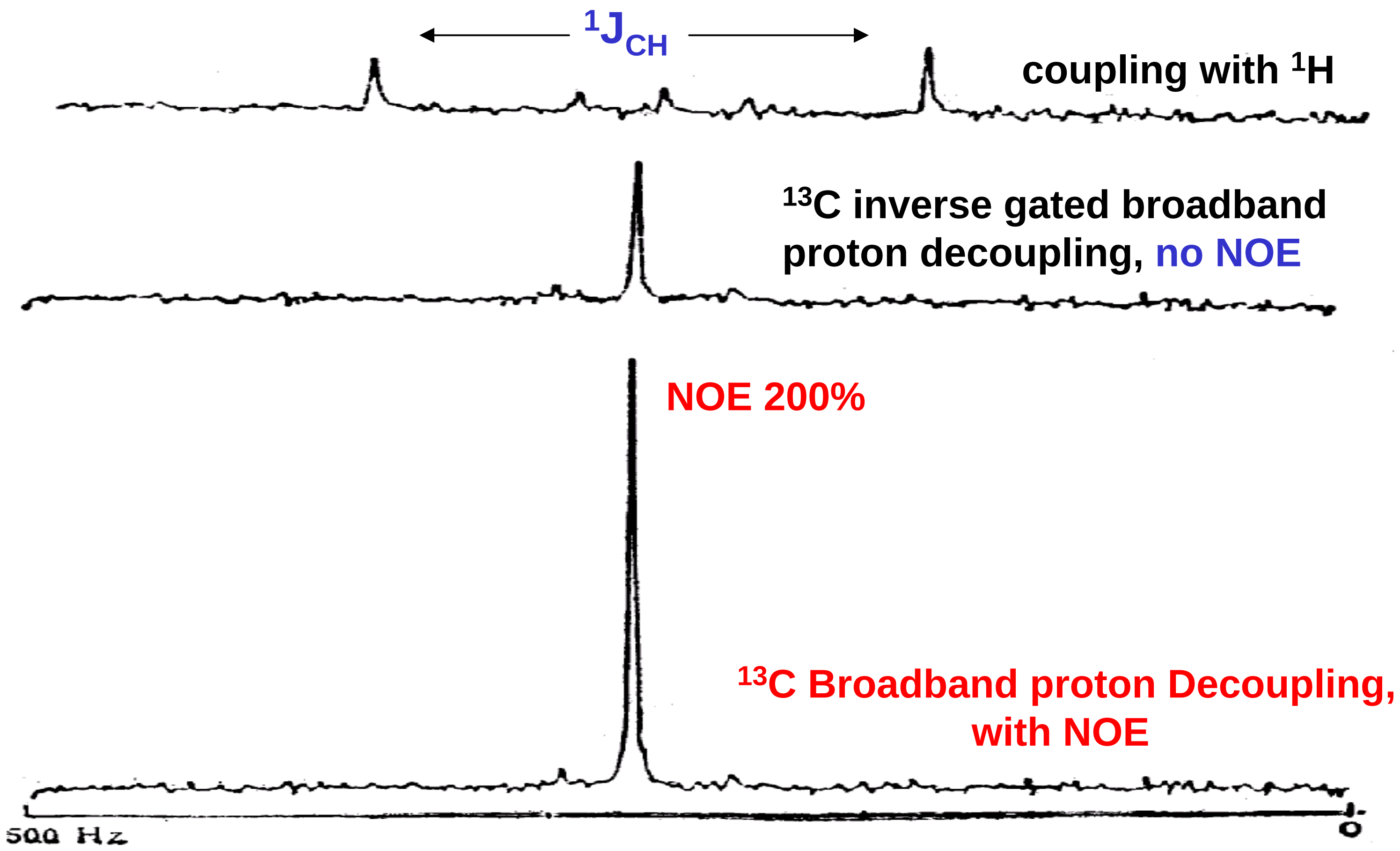
Coupling Constants for ^{2}H Coupled to ^{13}C

Compound	$^1J_{CD}$ ^1J (Hz)
$CDCl_3$	31.5
$CD_3C(=O)CD_3$	19.5
$(CD_3)_2SO$	22.0
	25.5

NOE Difference Spectra

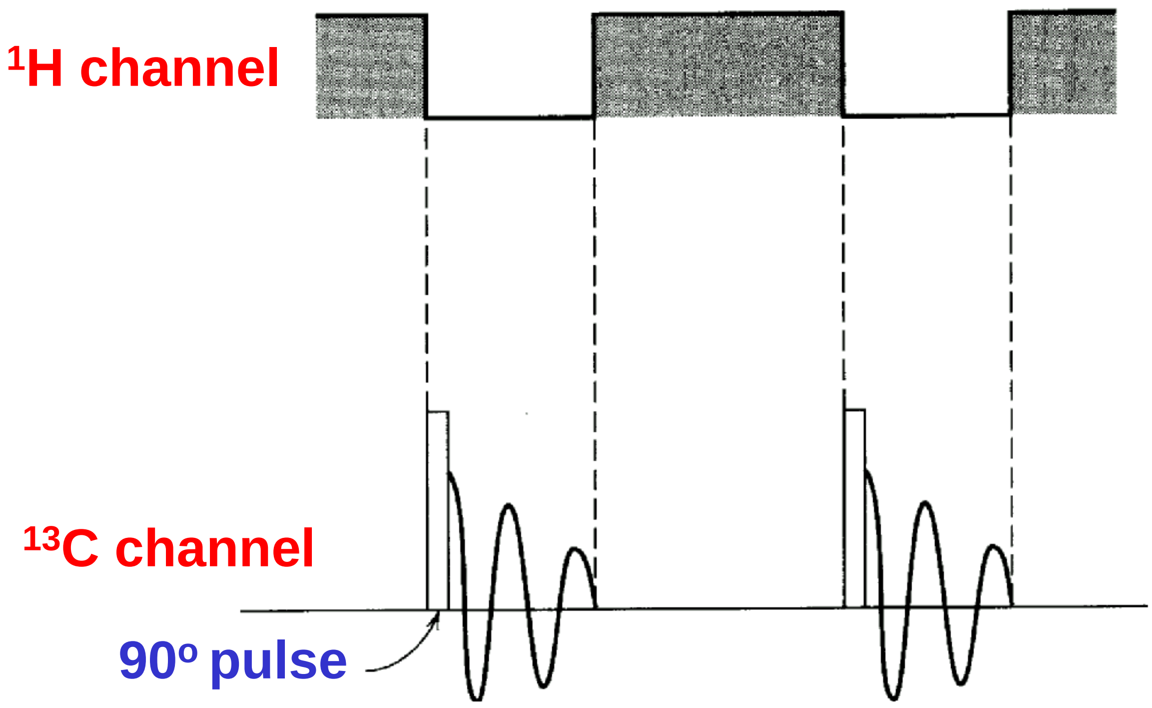


^{13}C NOE Effect of $CHCl_3$



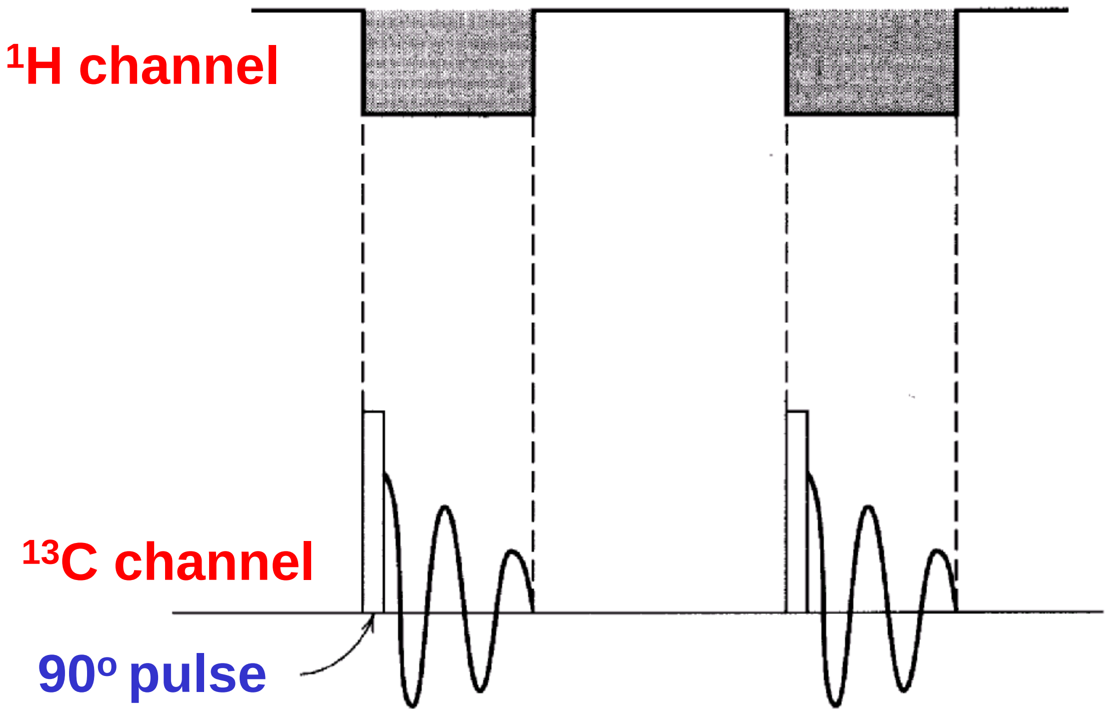
^{13}C Gated Decoupling technique

to retain at least part of the NOE and still maintain ^{13}C-^{1}H coupling



^{13}C Inverse Gated Broadband proton Decoupling

to deal with the NOE

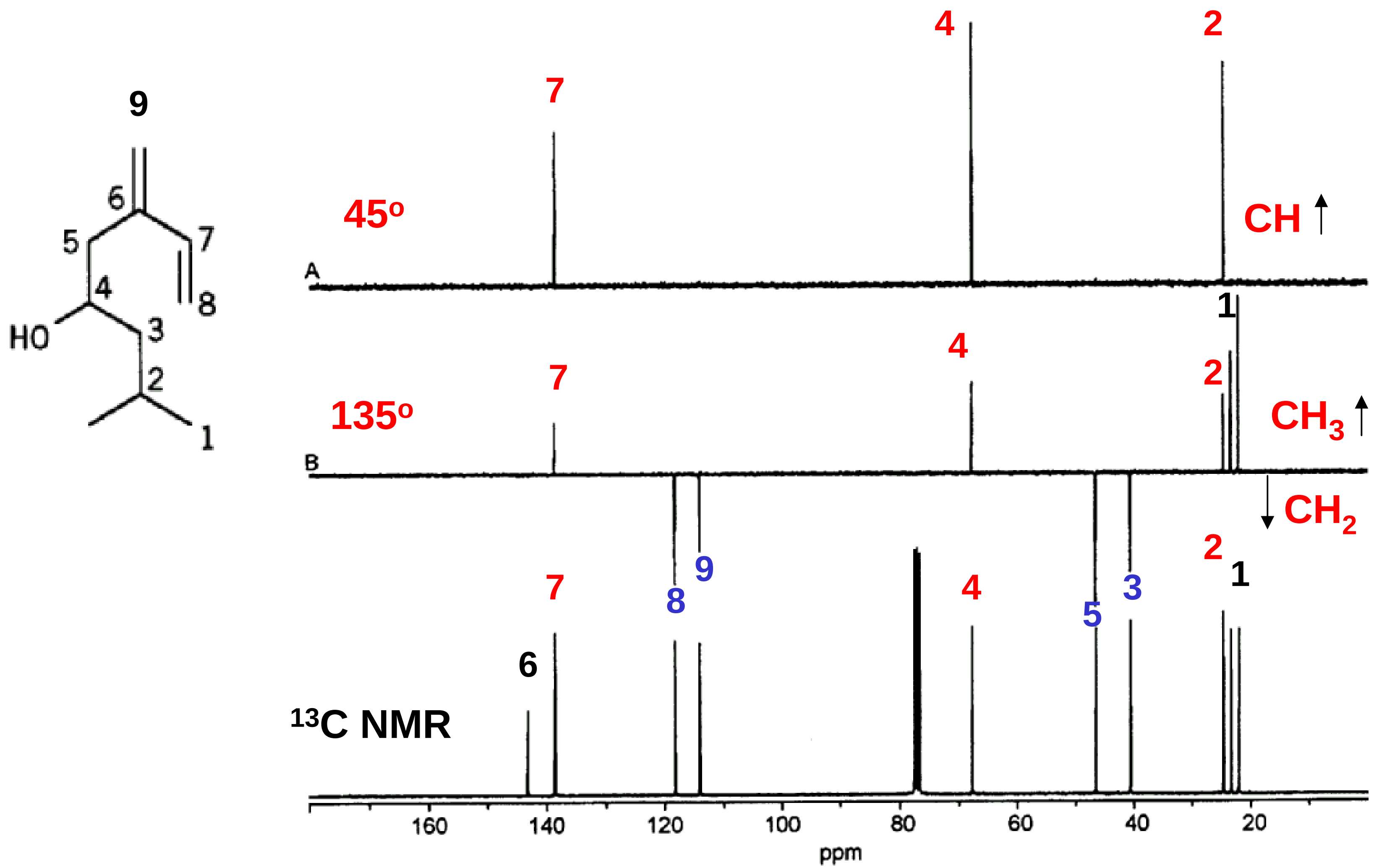


DEPT Spectra

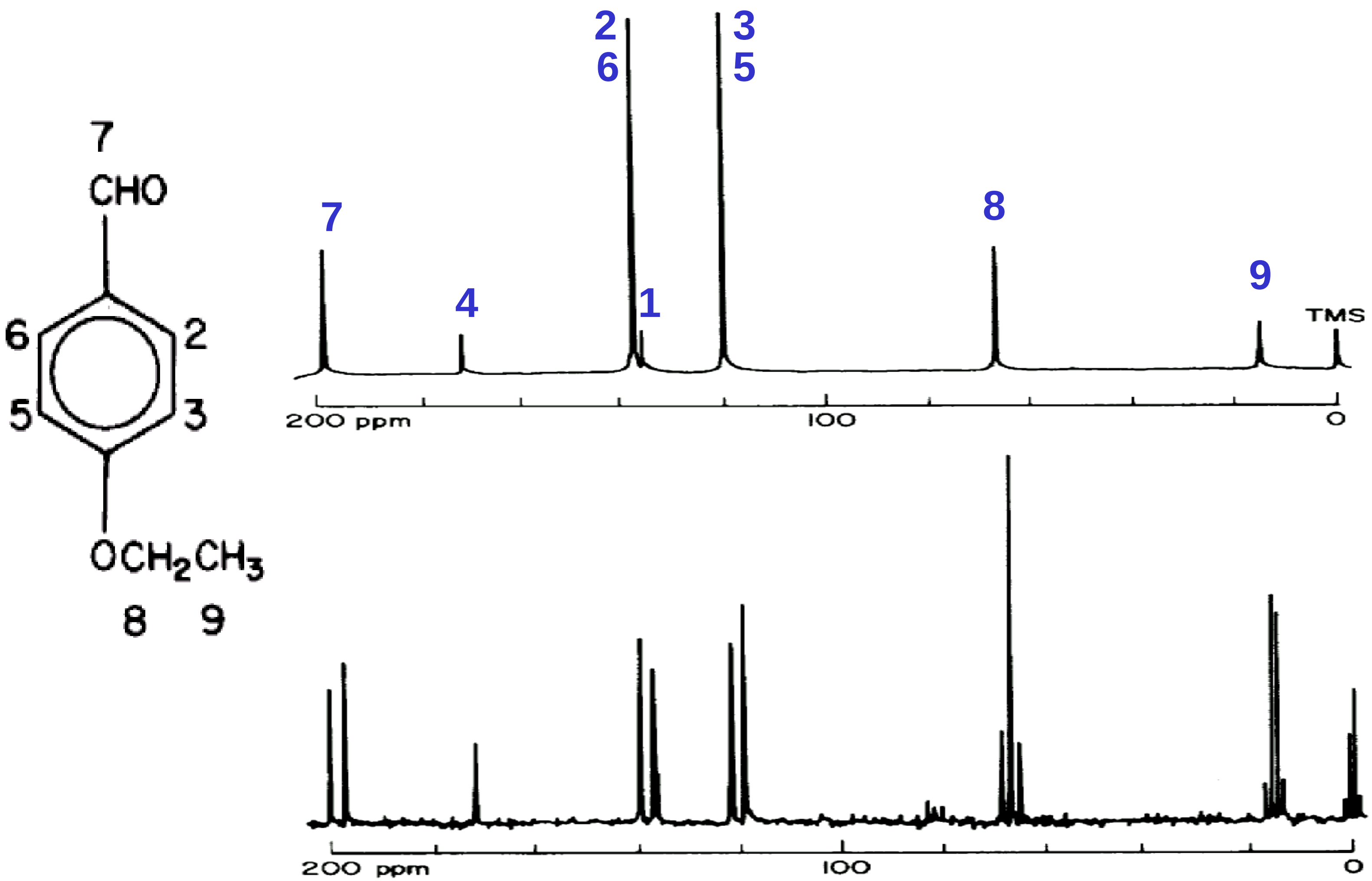
(Distortionless Enhancement by Polarizatin Transfer)

distinguishing between CH_3, CH_2 and CH

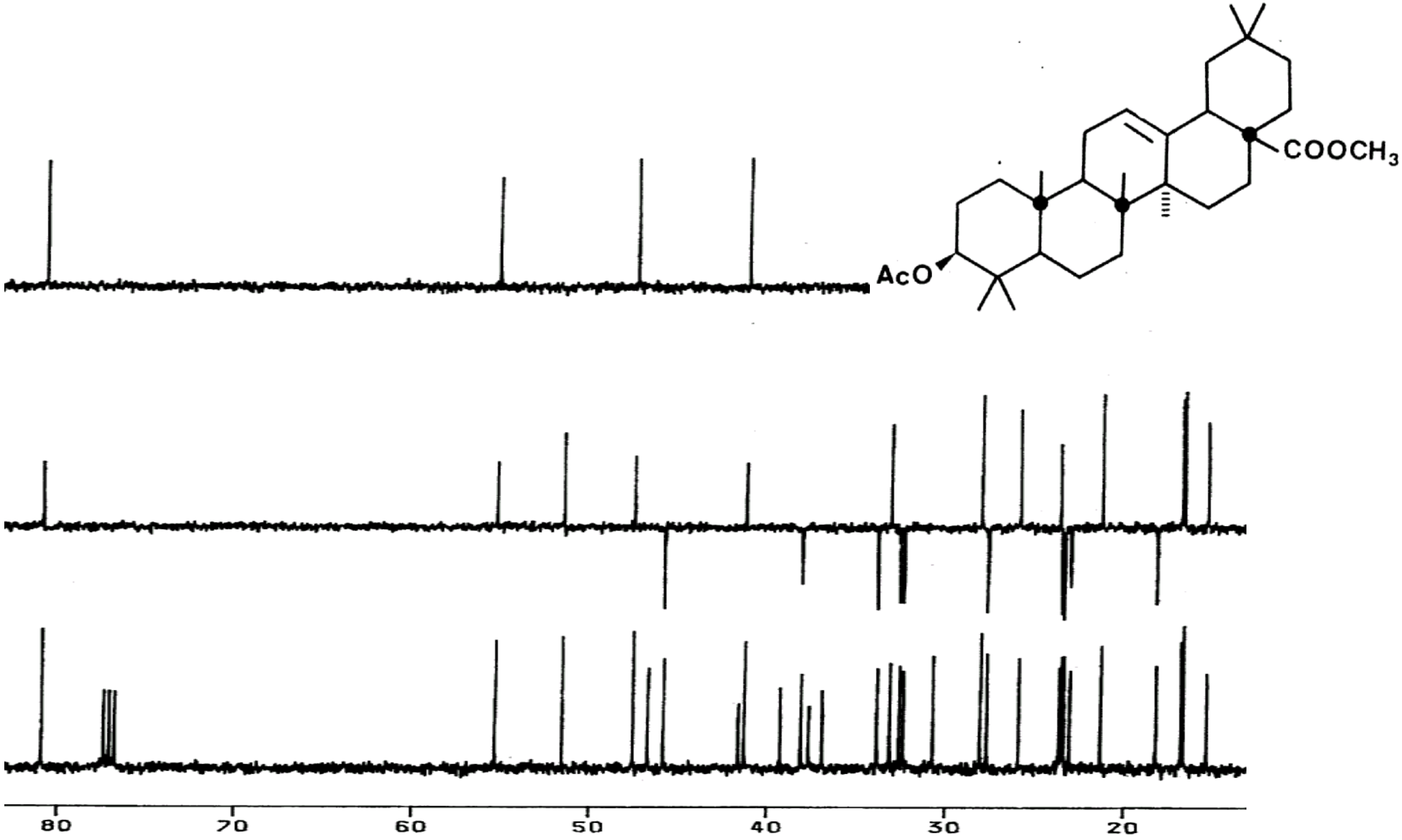
(replacement for " off- resonance decoupling")



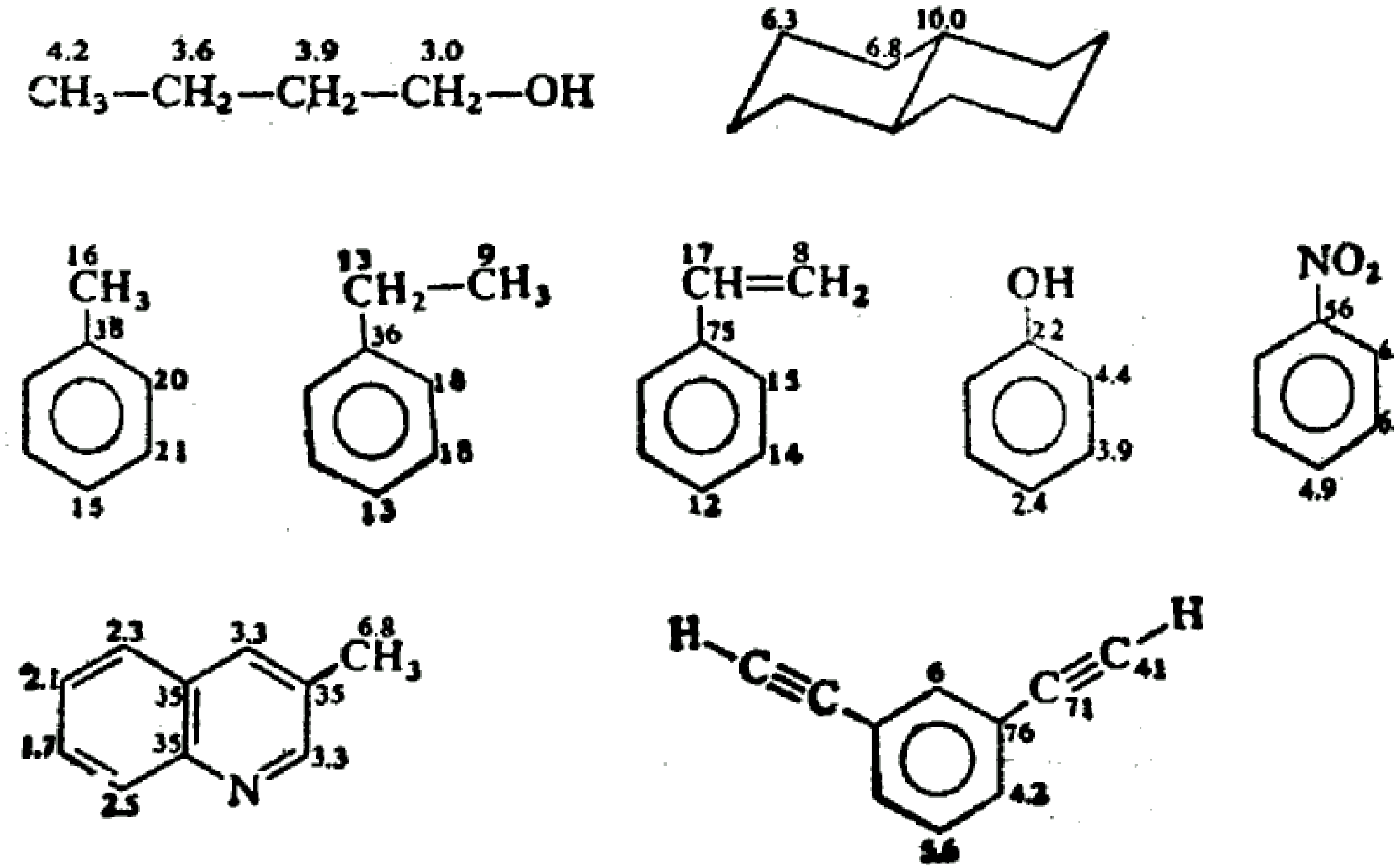
^{13}C "Off-Resonance Decoupling"



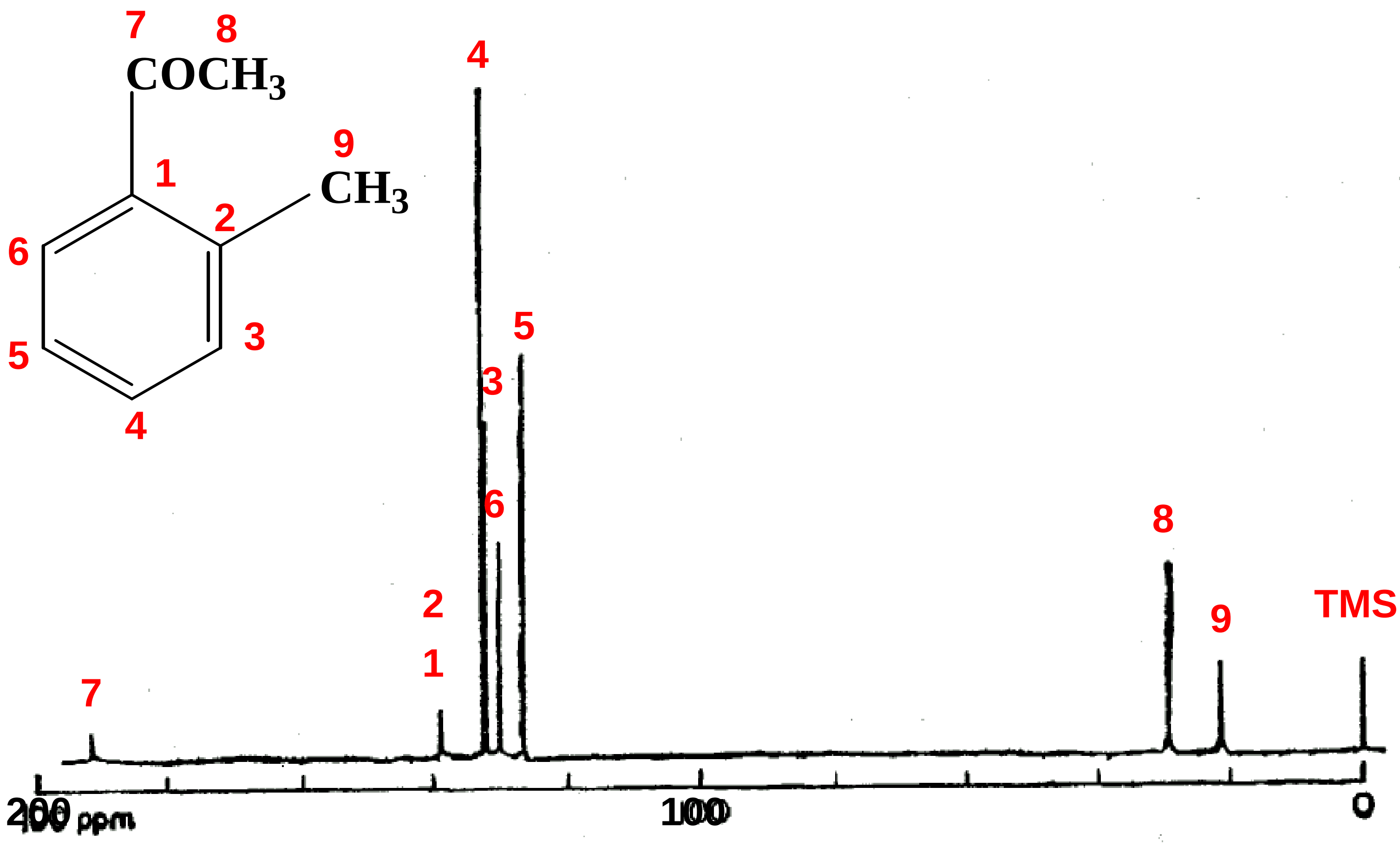
DEPT Spectrum, an example



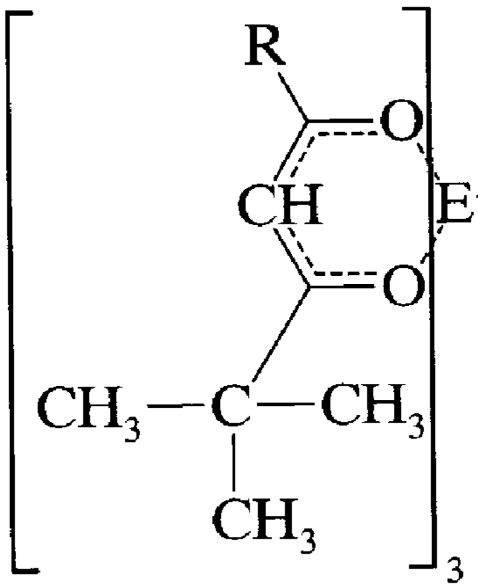
^{13}C Relaxation Time (T_1 of 10^{-3} – 10^{3} sec)

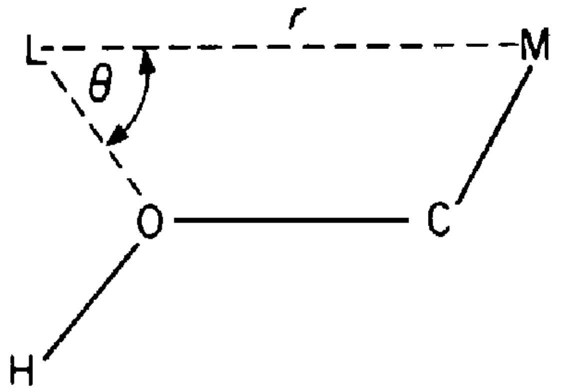


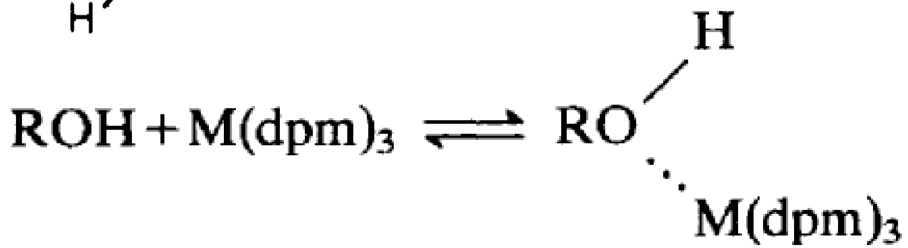
^{13}C Relaxation Time (T_1): An Example



NMR Shift Reagents





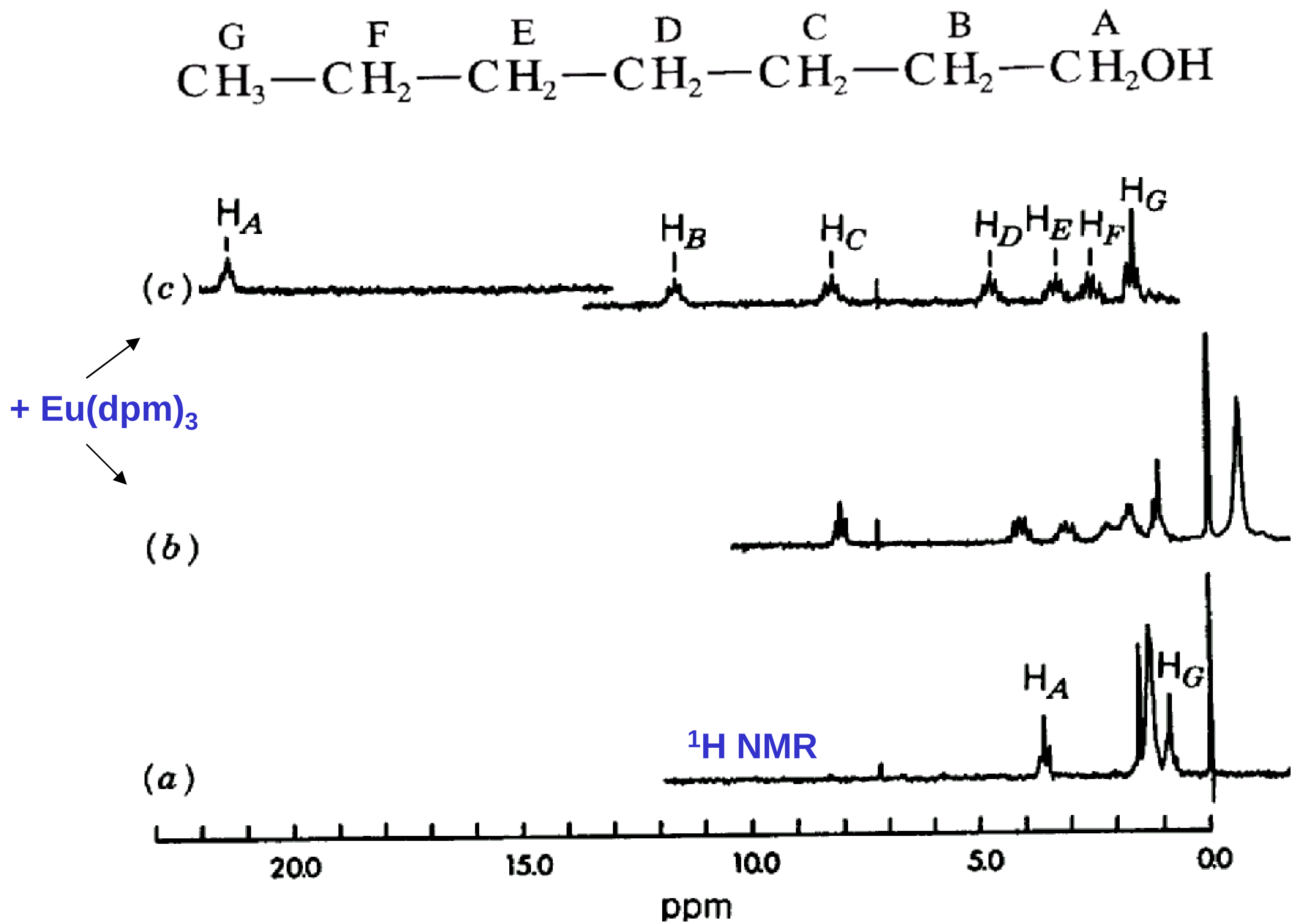


R = t-butyl, Eu(dpm)$_3$

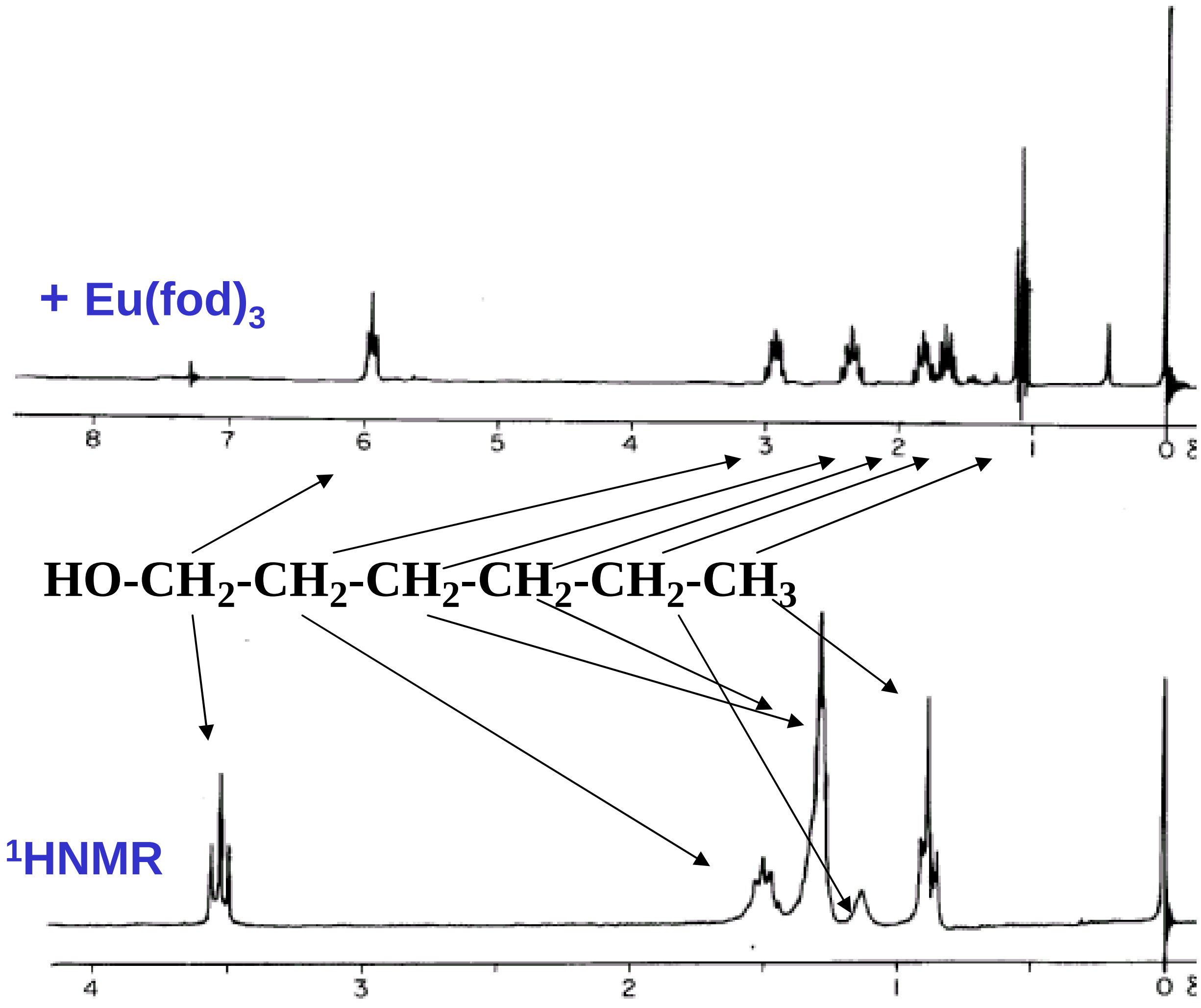
R = $CF_2CF_2CF_3$, Eu or Pr(fod)$_3$

M = Eu or Pr

NMR Shift Reagents



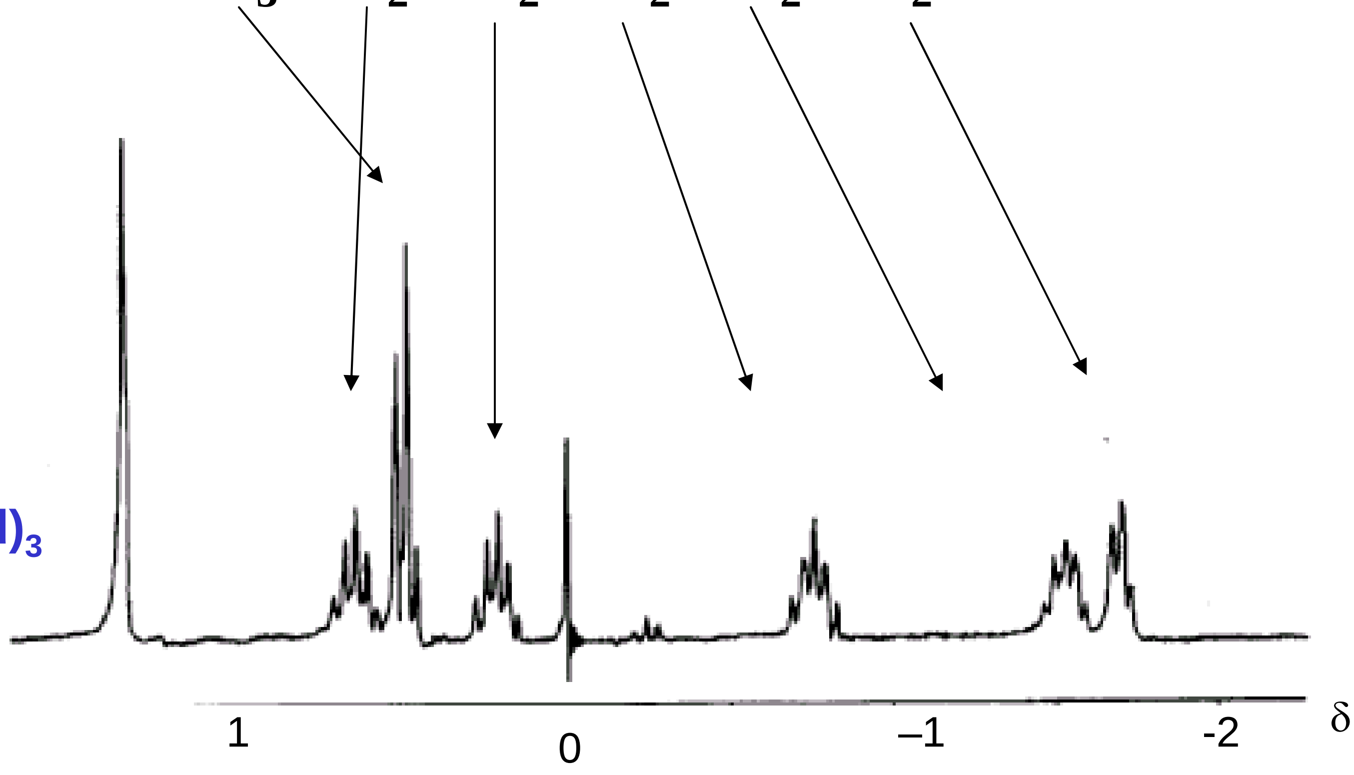
NMR Shift Reagents



NMR Shift Reagents

CH_3-CH_2-CH_2-CH_2-CH_2-CH_2-OH

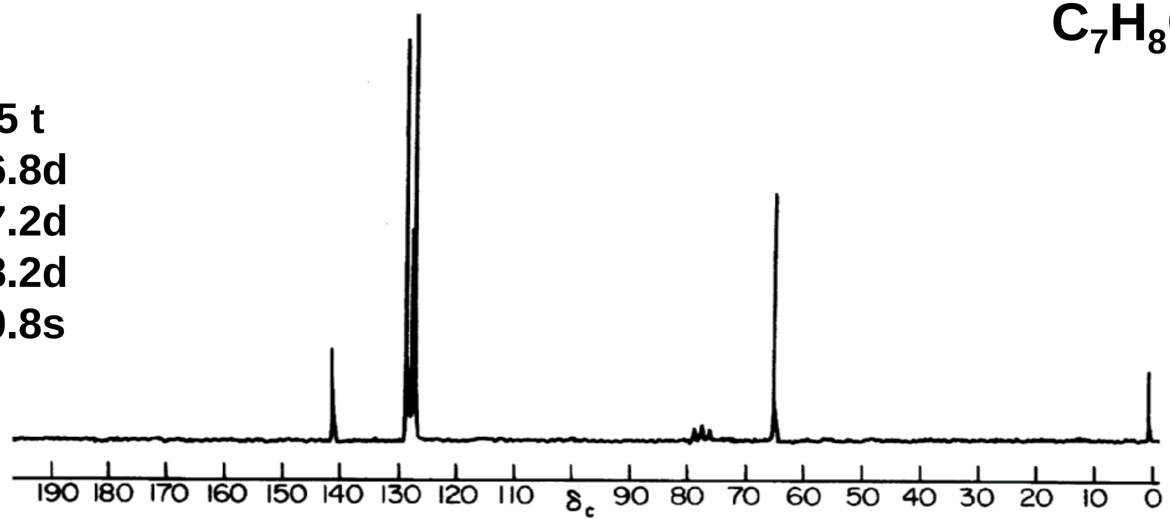
+ $Pr(fod)_3$

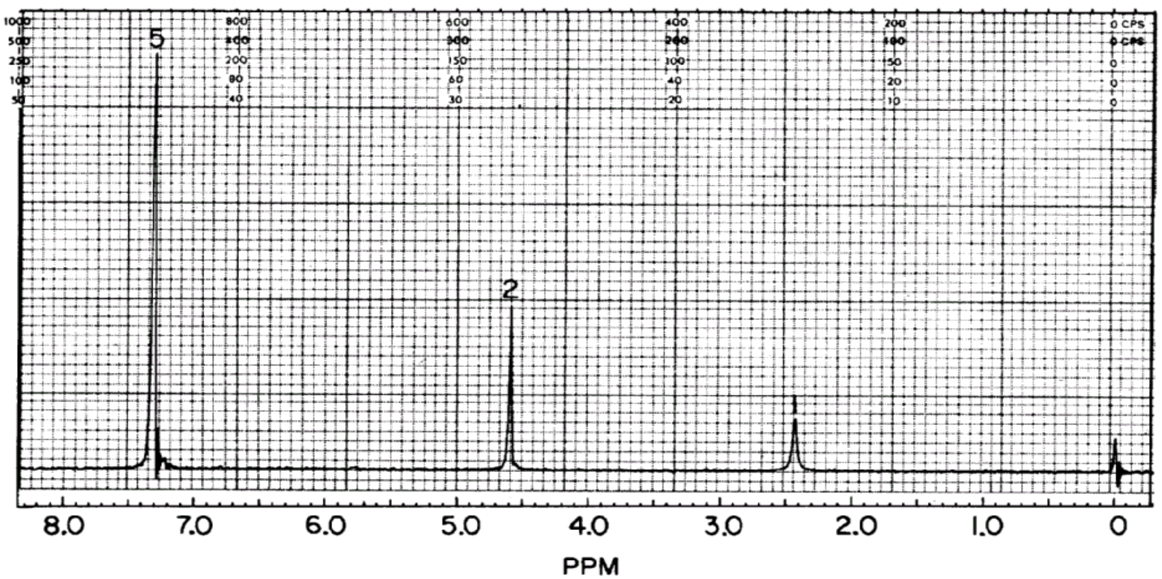


Chapter 5: Structural Elucidation by Using 1D NMR Spectroscopy

C_7H_8O

64.5 t
126.8d
127.2d
128.2d
140.8s





Unsaturation Number: Index of Hydrogen Deficiency

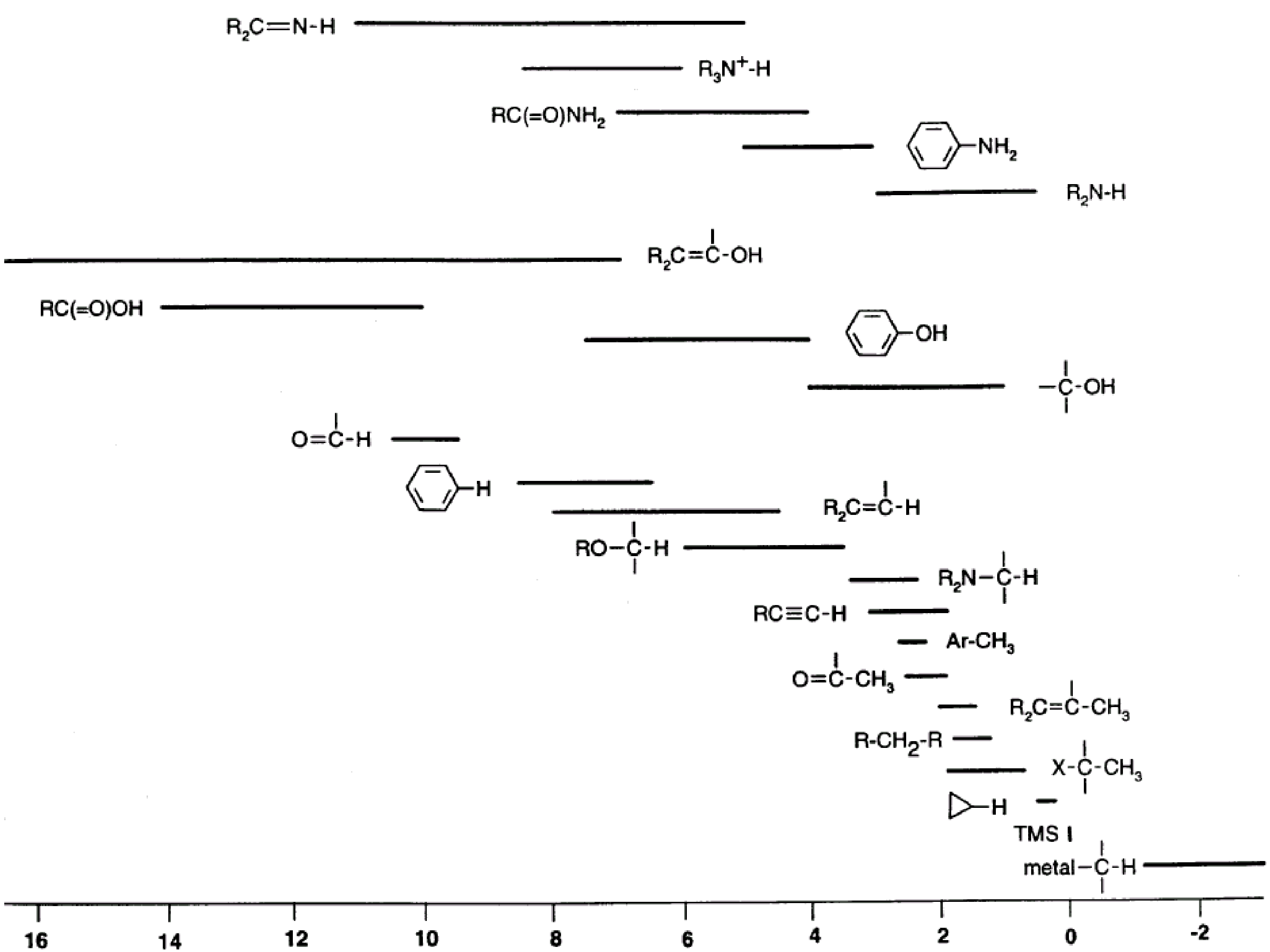
$$\Omega = C + 1 - H/2 - X/2 + N/2$$

(X = F, Cl, Br, I)

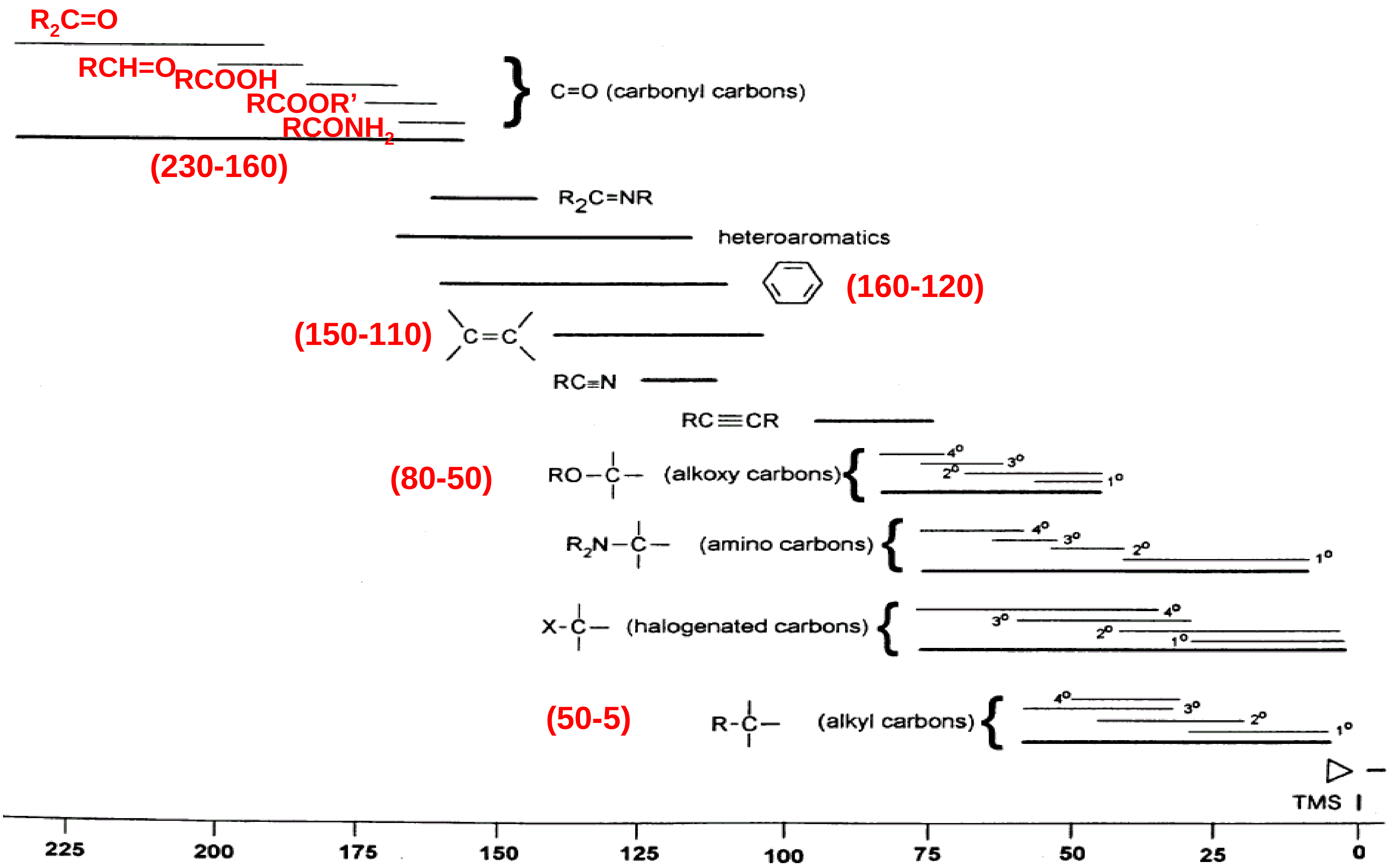
For example: C_7H_8O

$$\Omega = C + 1 - H/2 - X/2 + N/2$$
$$= 7 + 1 - 8/2 = 4$$

^{1}H Chemical Shifts of Common Structures



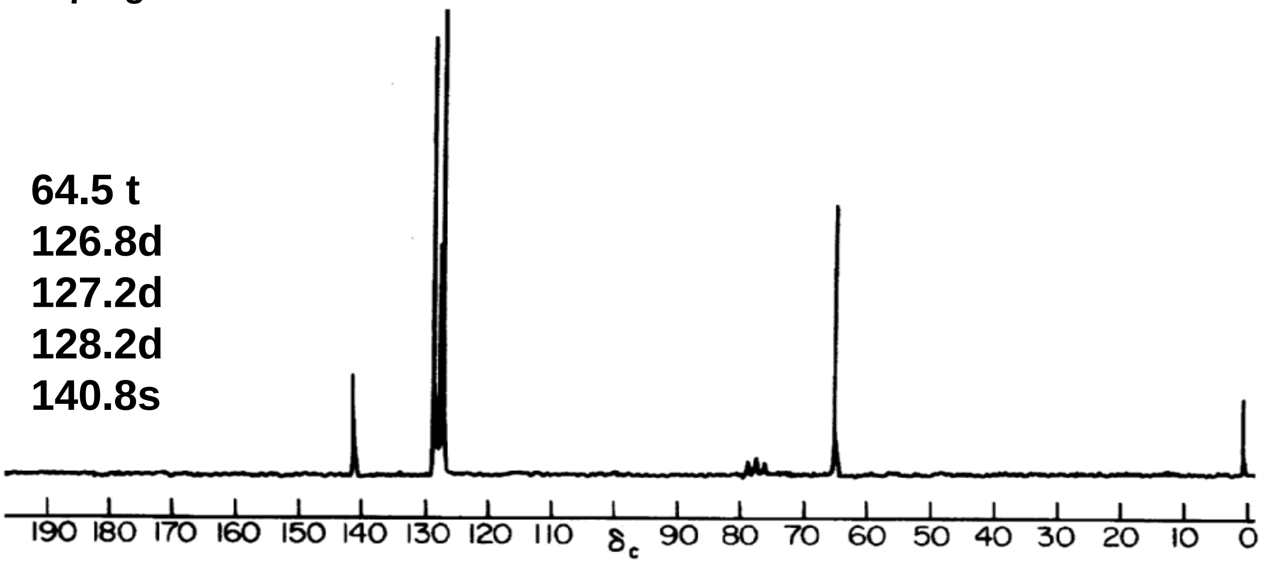
^{13}C Chemical Shifts of Common Structures

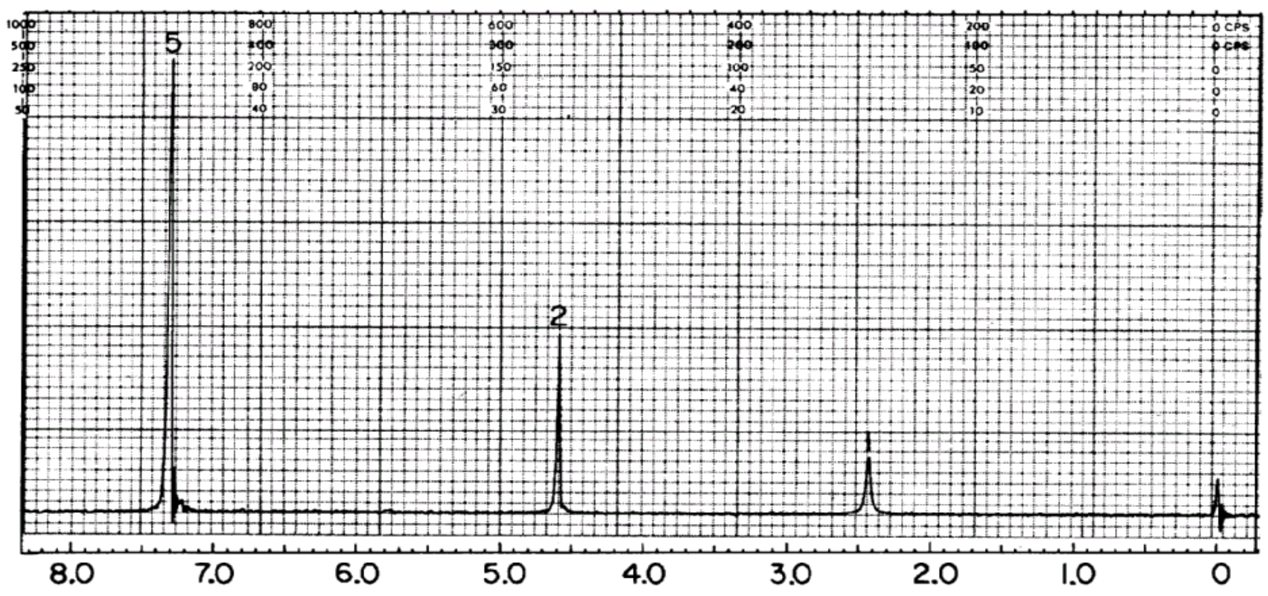


Problem 1

C_7H_8O

64.5 t
126.8d
127.2d
128.2d
140.8s



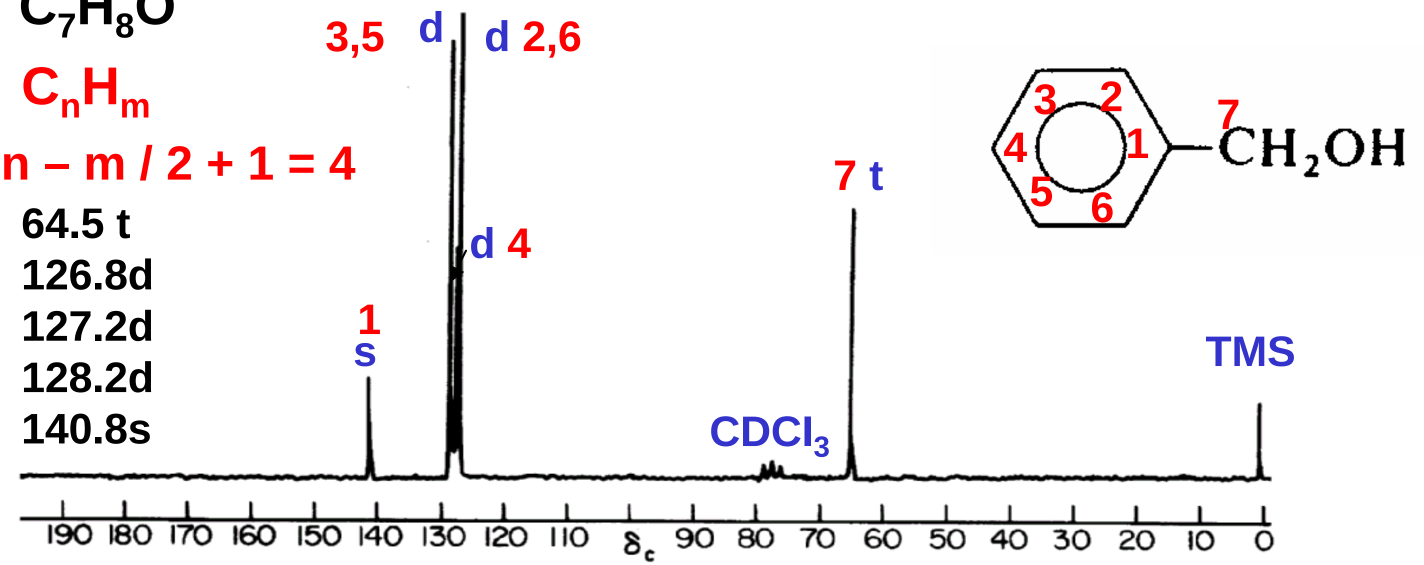


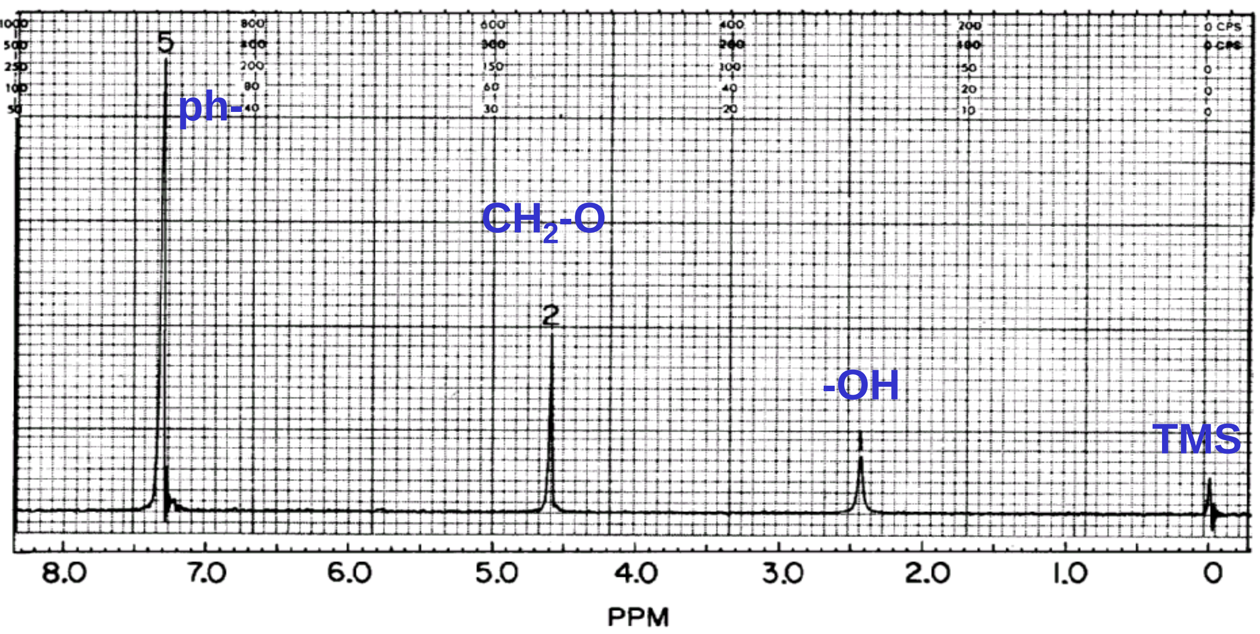
C_7H_8O

C_nH_m

$\Omega = n - m / 2 + 1 = 4$

64.5 t
126.8d
127.2d
128.2d
140.8s

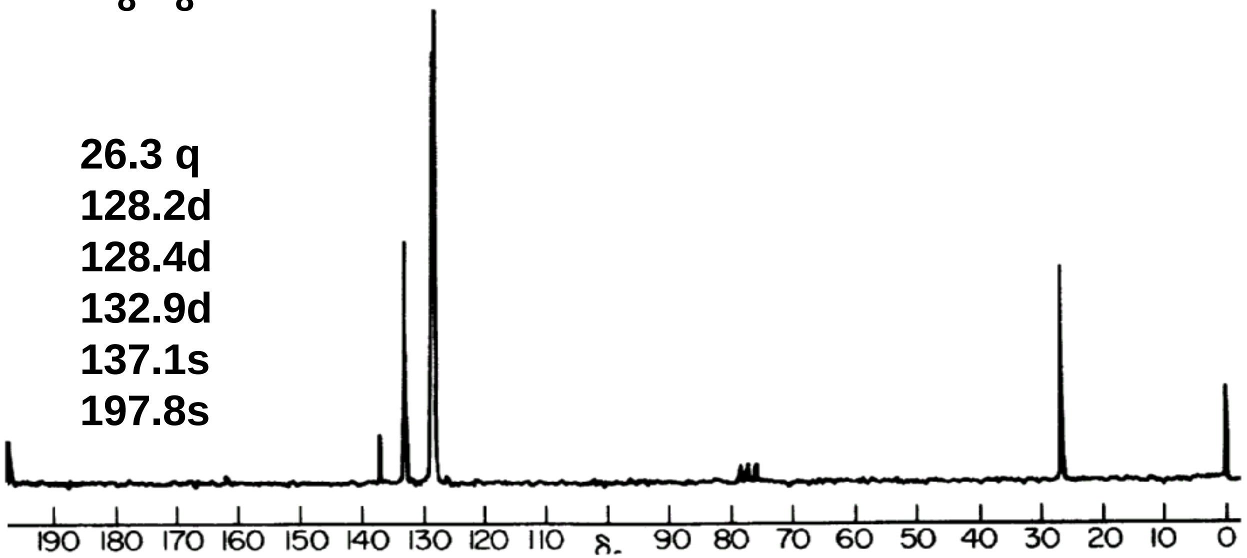


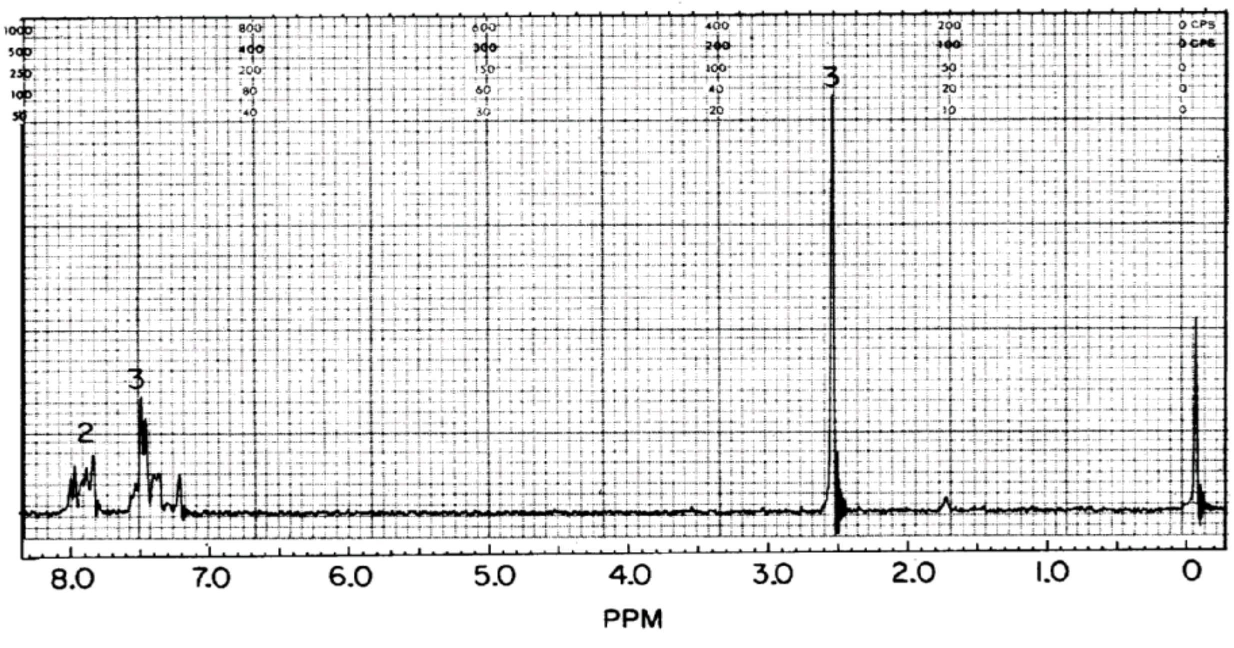


Problem 2

C_8H_8O

26.3 q
128.2d
128.4d
132.9d
137.1s
197.8s

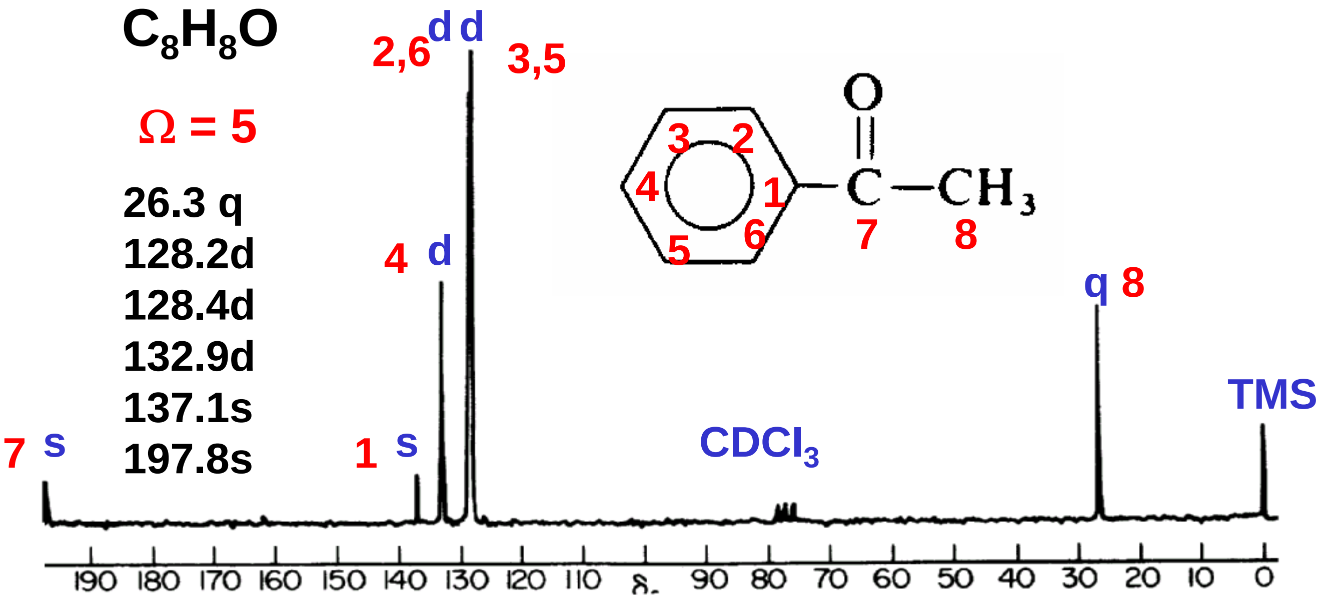


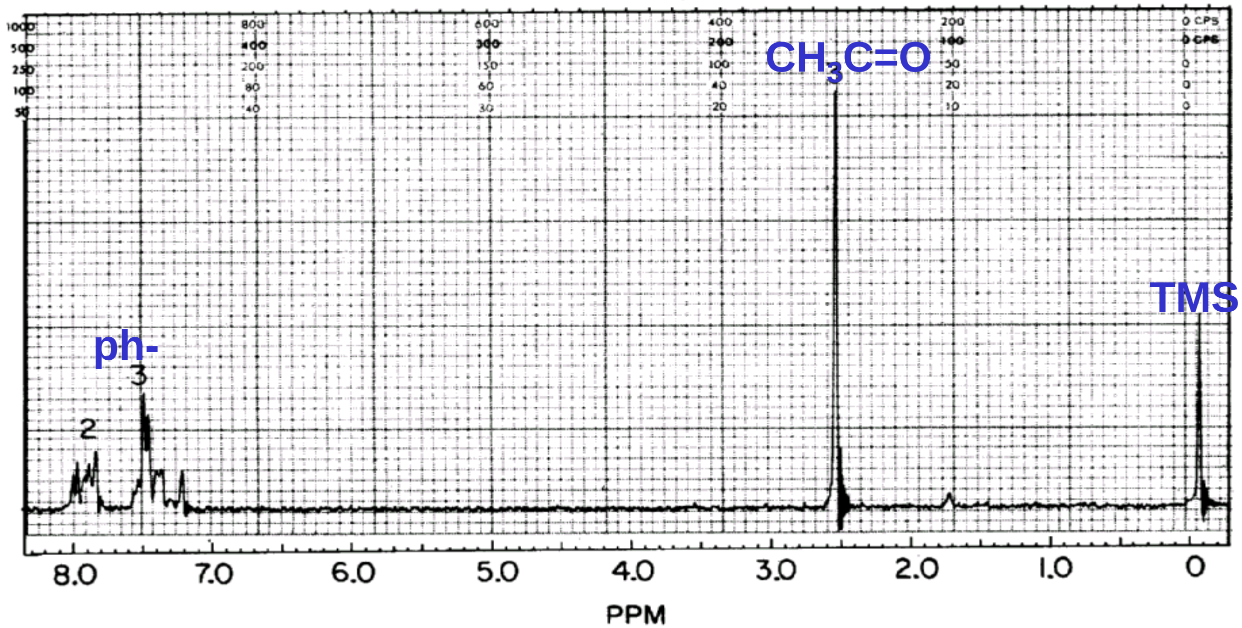


C_8H_8O

$\Omega = 5$

26.3 q
128.2d
128.4d
132.9d
137.1s
197.8s

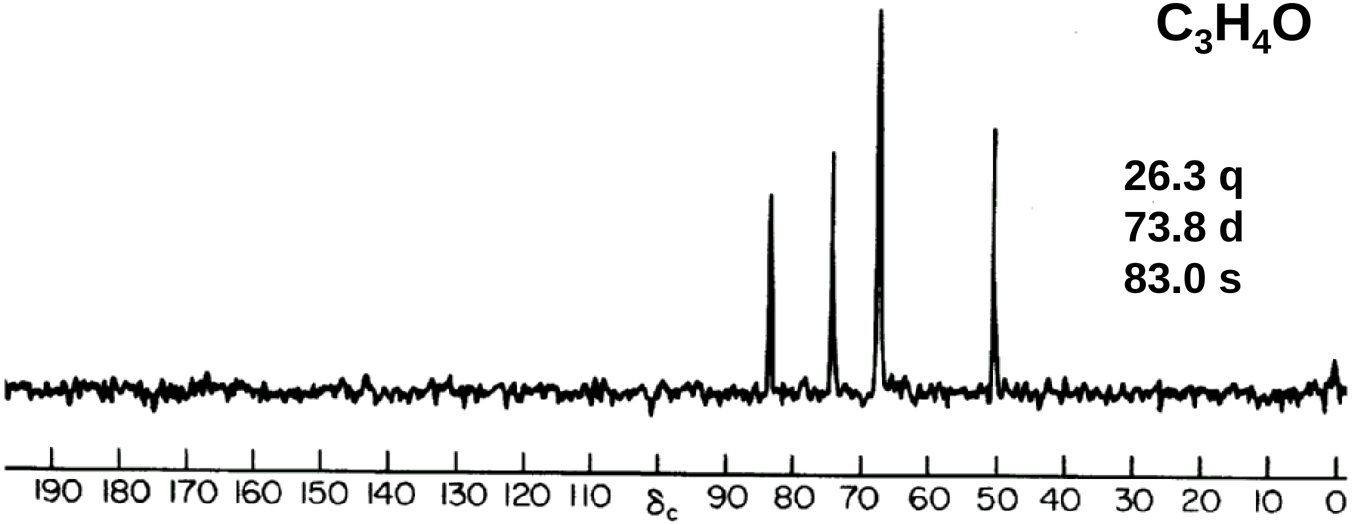


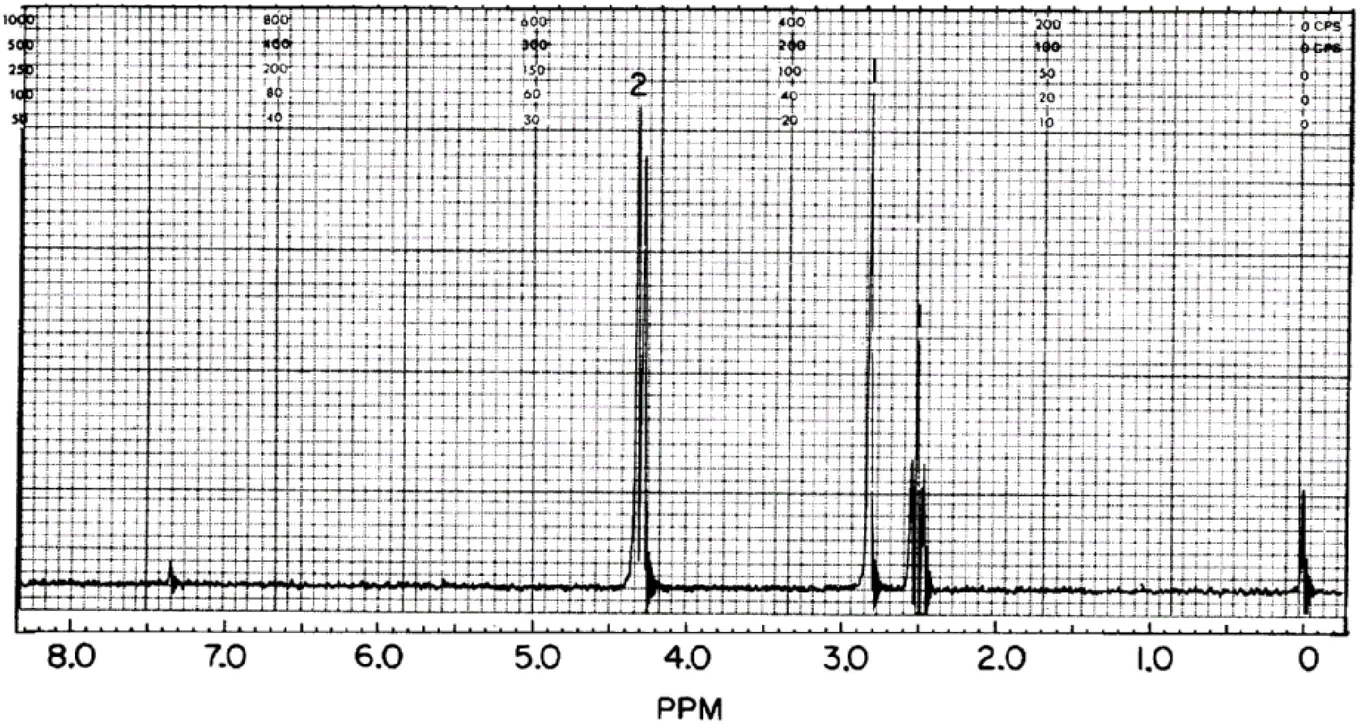


Problem 3

C_3H_4O

26.3 q
73.8 d
83.0 s



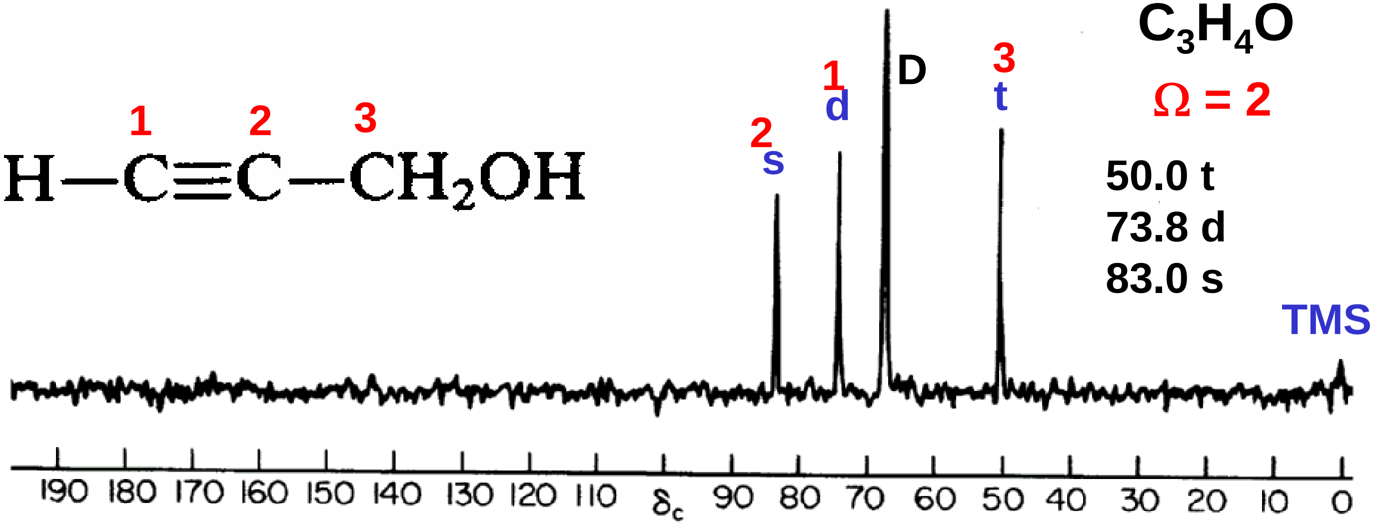


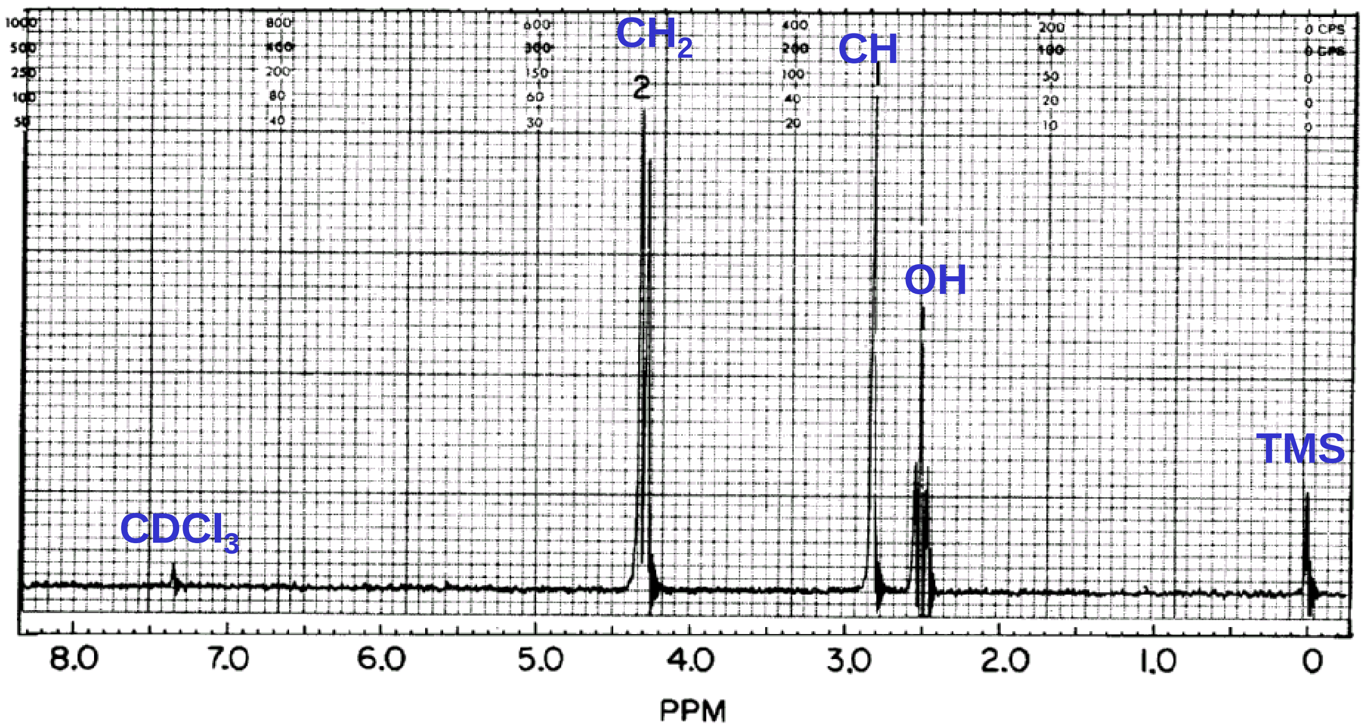
$H-C \equiv C-CH_2OH$ (carbons numbered 1, 2, 3)

C_3H_4O

$\Omega = 2$

50.0 t
73.8 d
83.0 s

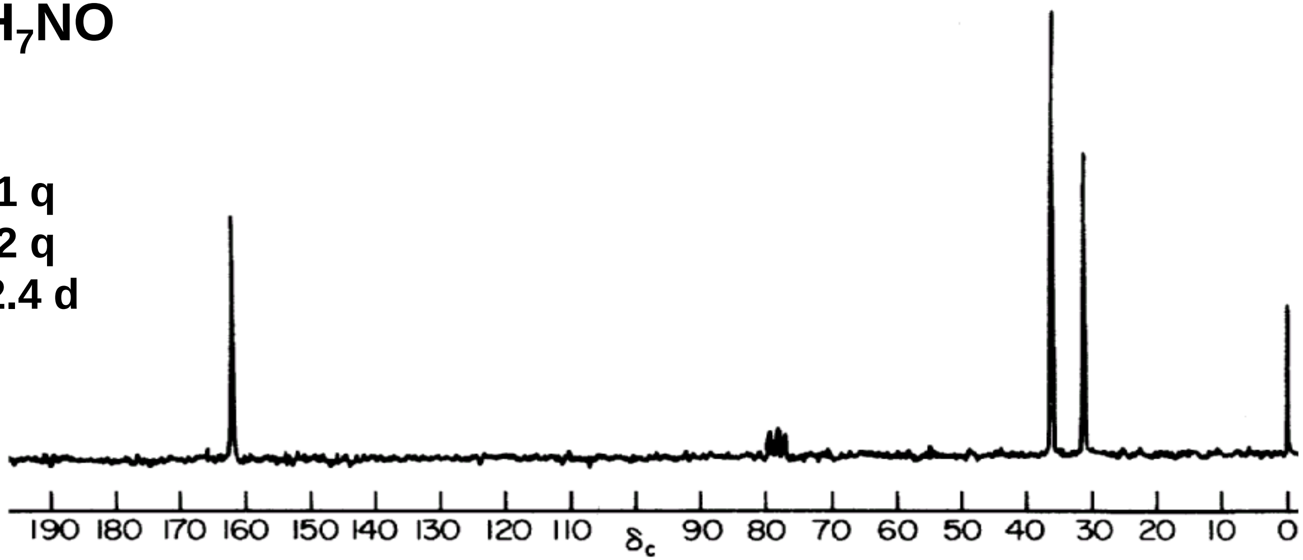


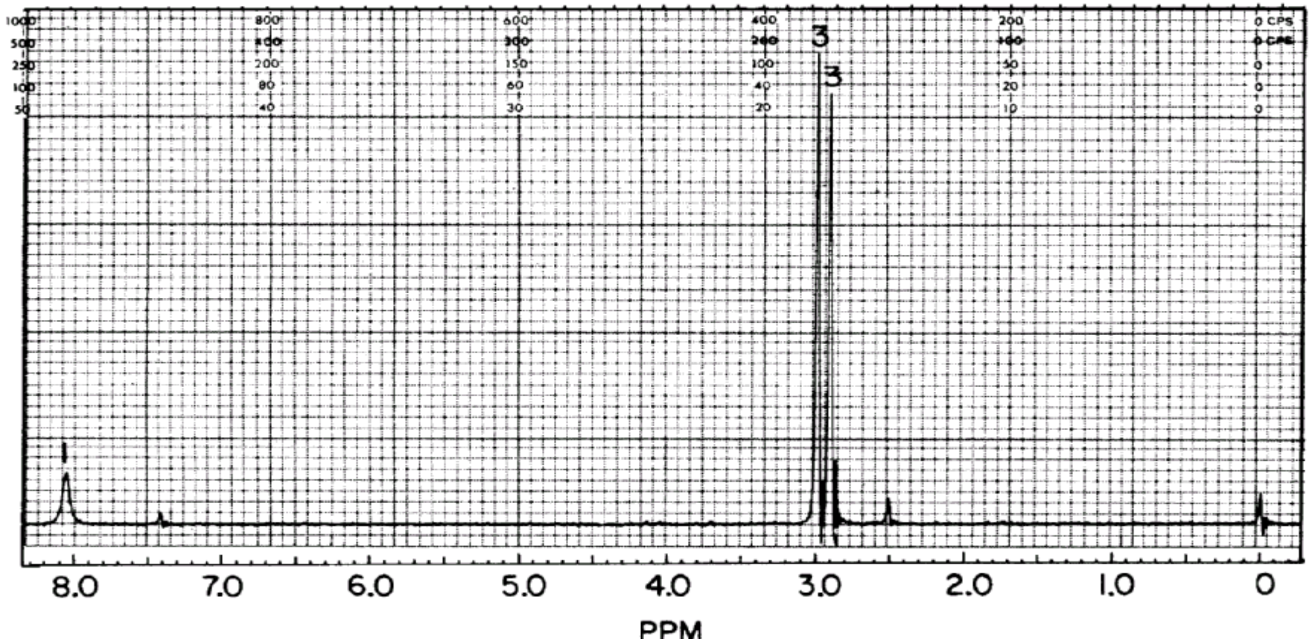


Problem 4

C_3H_7NO

31.1 q
36.2 q
162.4 d

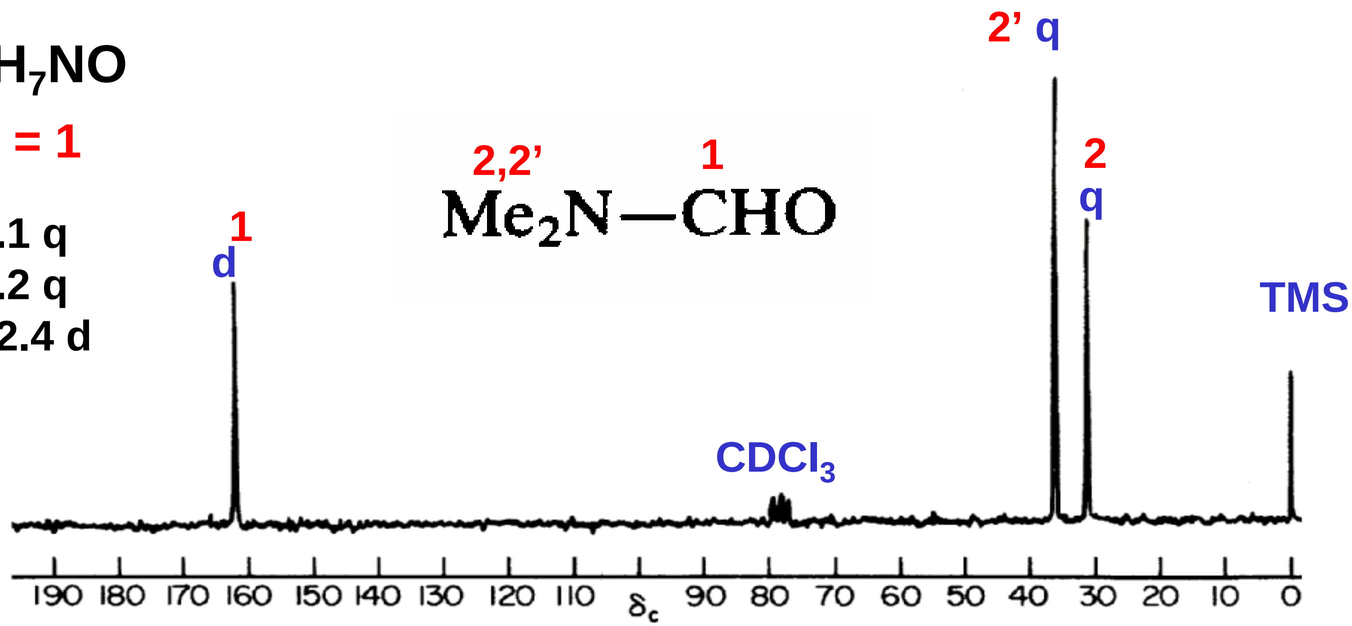


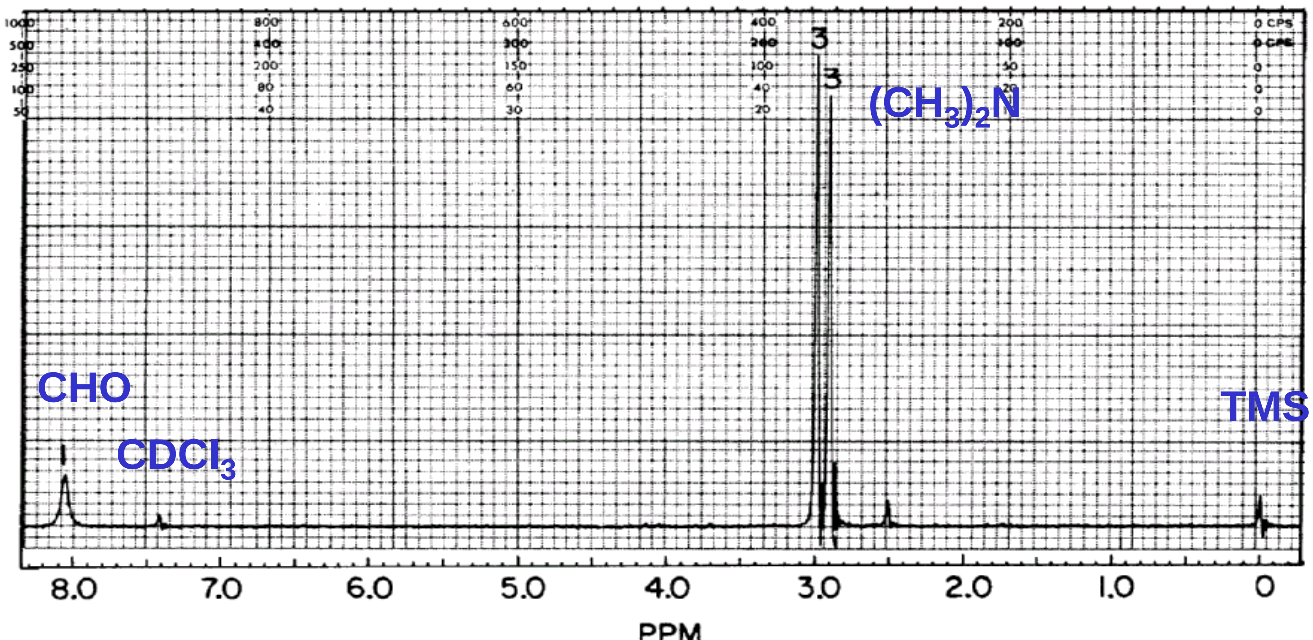


C_3H_7NO

$\Omega = 1$

31.1 q
36.2 q
162.4 d

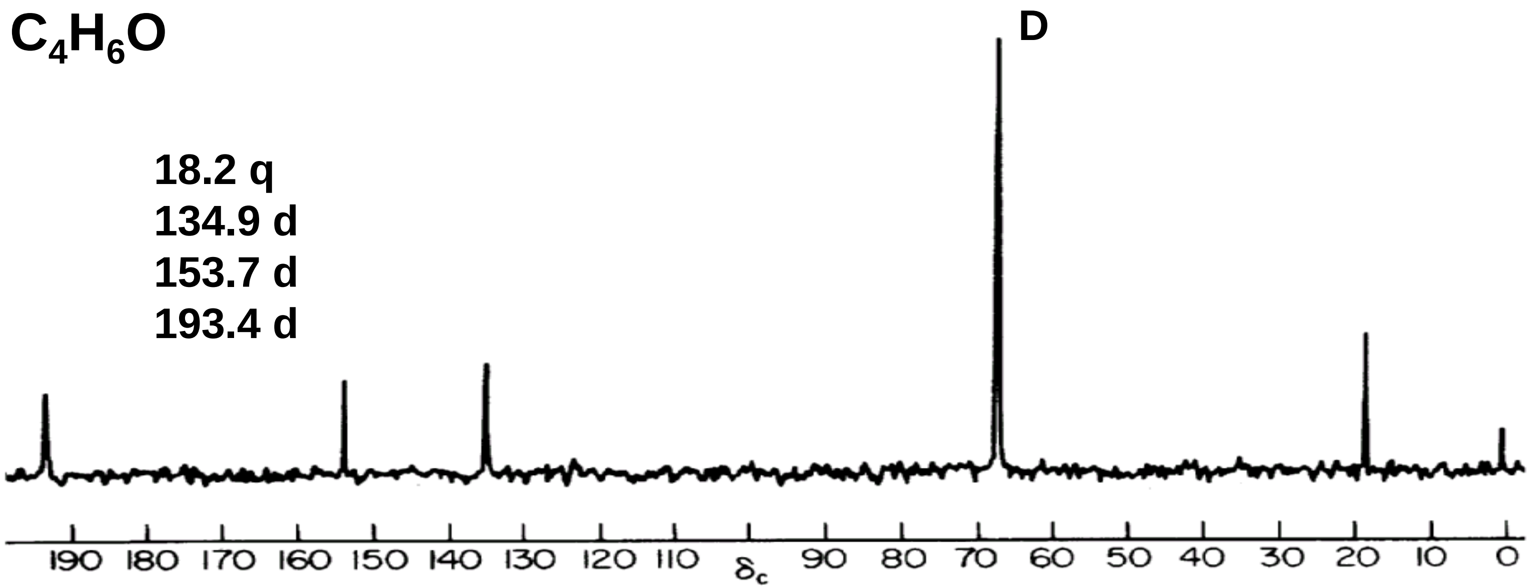


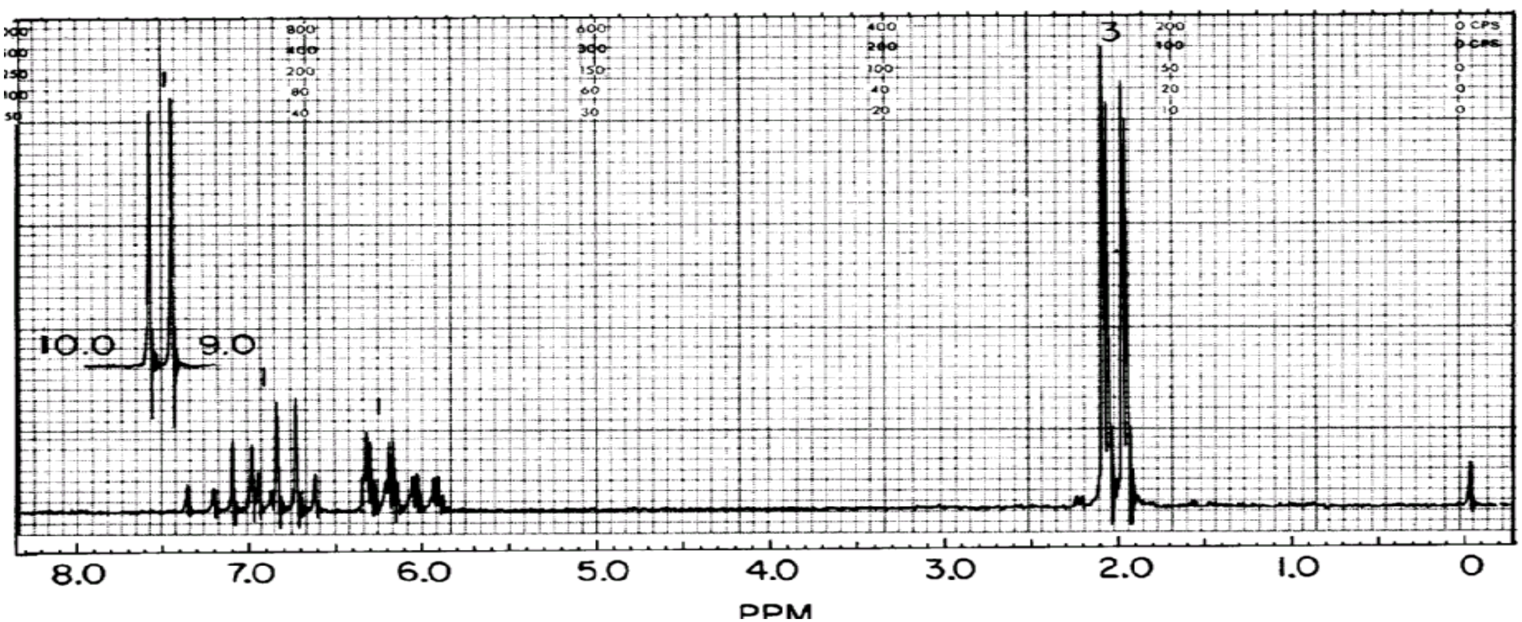


Problem 5

C_4H_6O

18.2 q
134.9 d
153.7 d
193.4 d



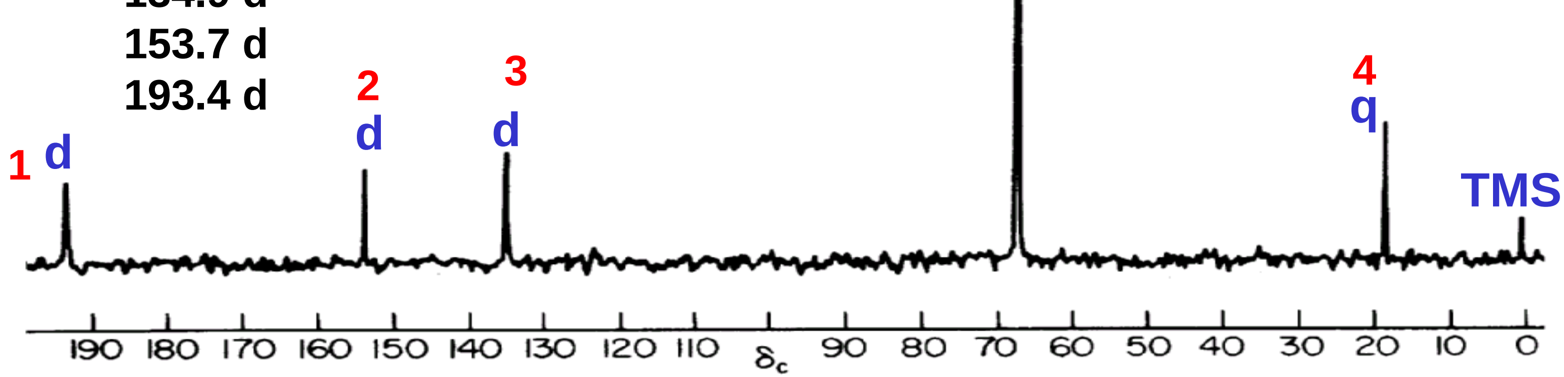


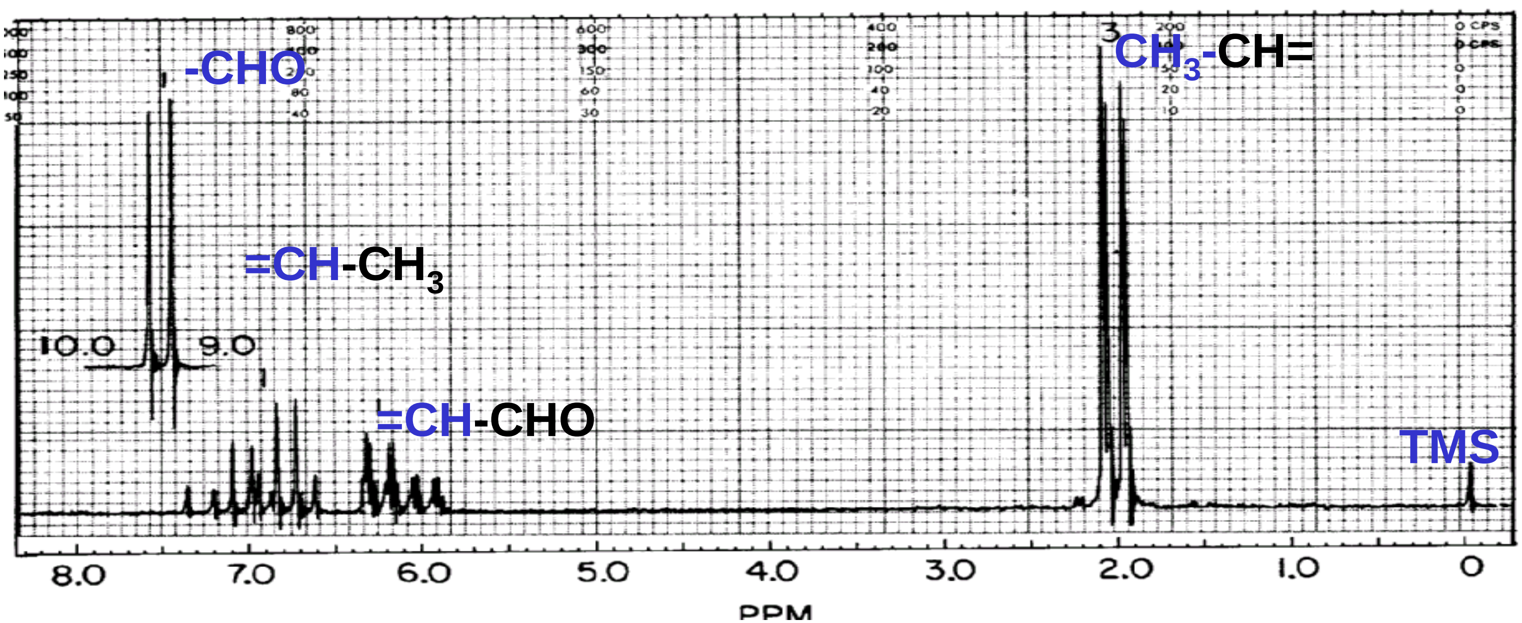
C_4H_6O

$\Omega = 2$

18.2 q
134.9 d
153.7 d
193.4 d

4 3 2 1
$CH_3CH{=}CH{-}CHO$

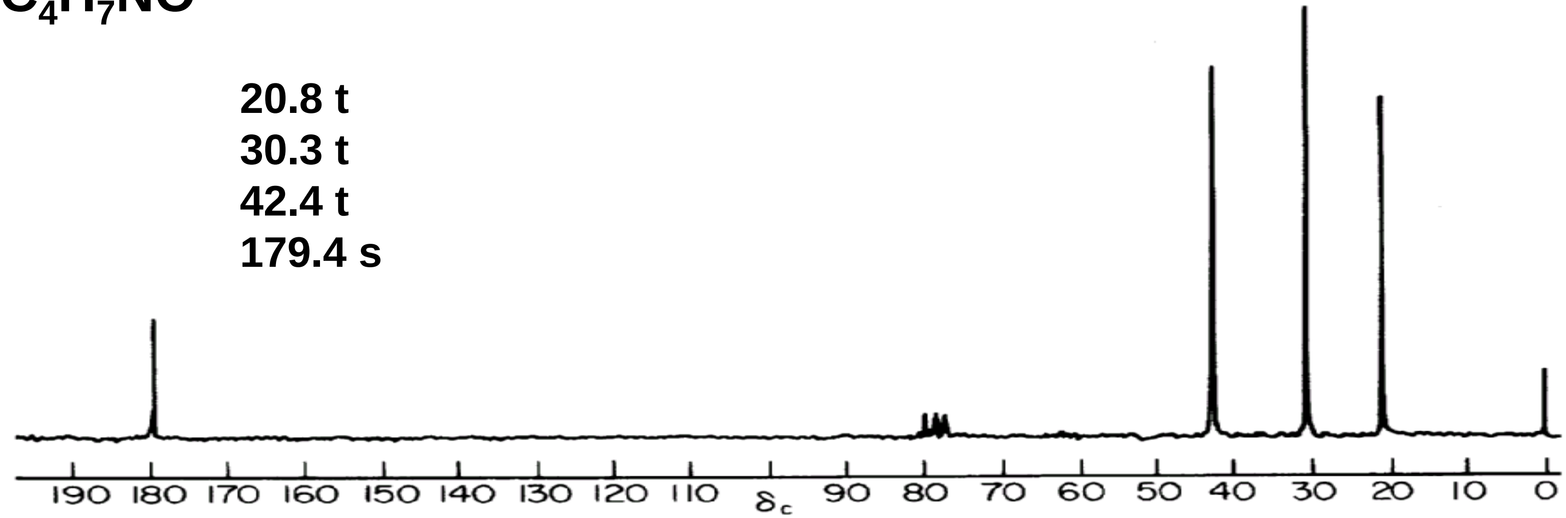


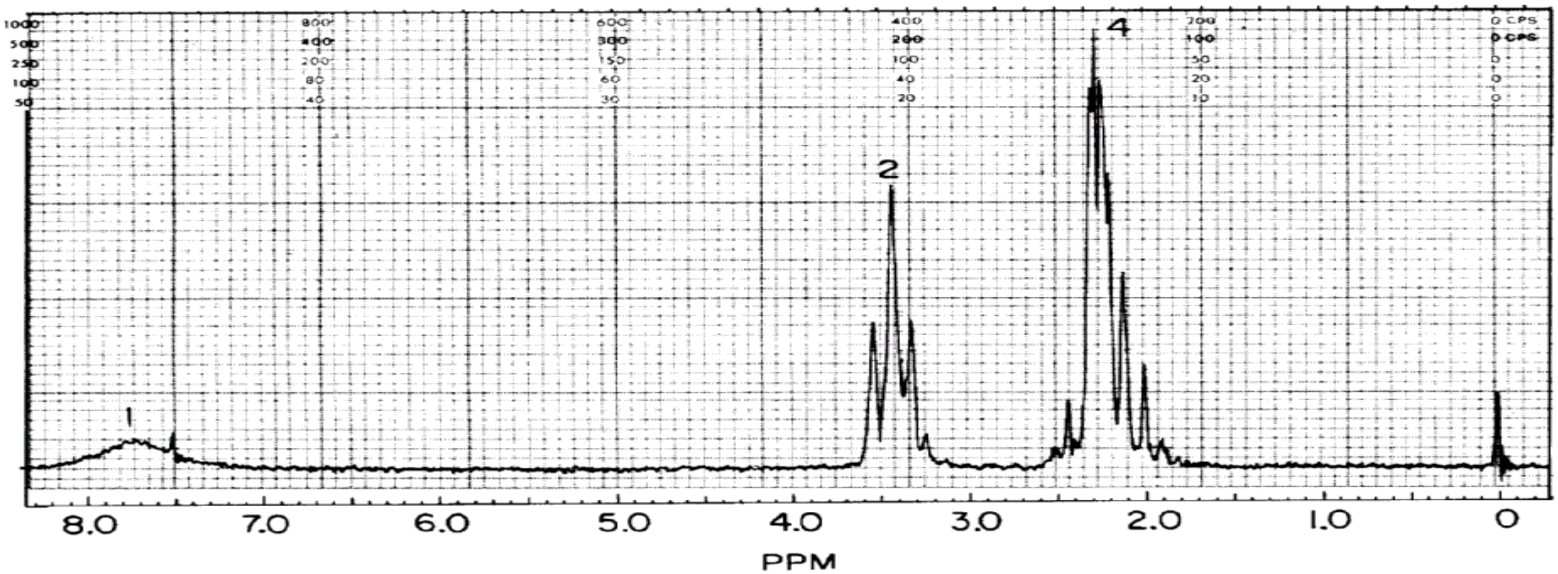


Problem 6

C_4H_7NO

20.8 t
30.3 t
42.4 t
179.4 s

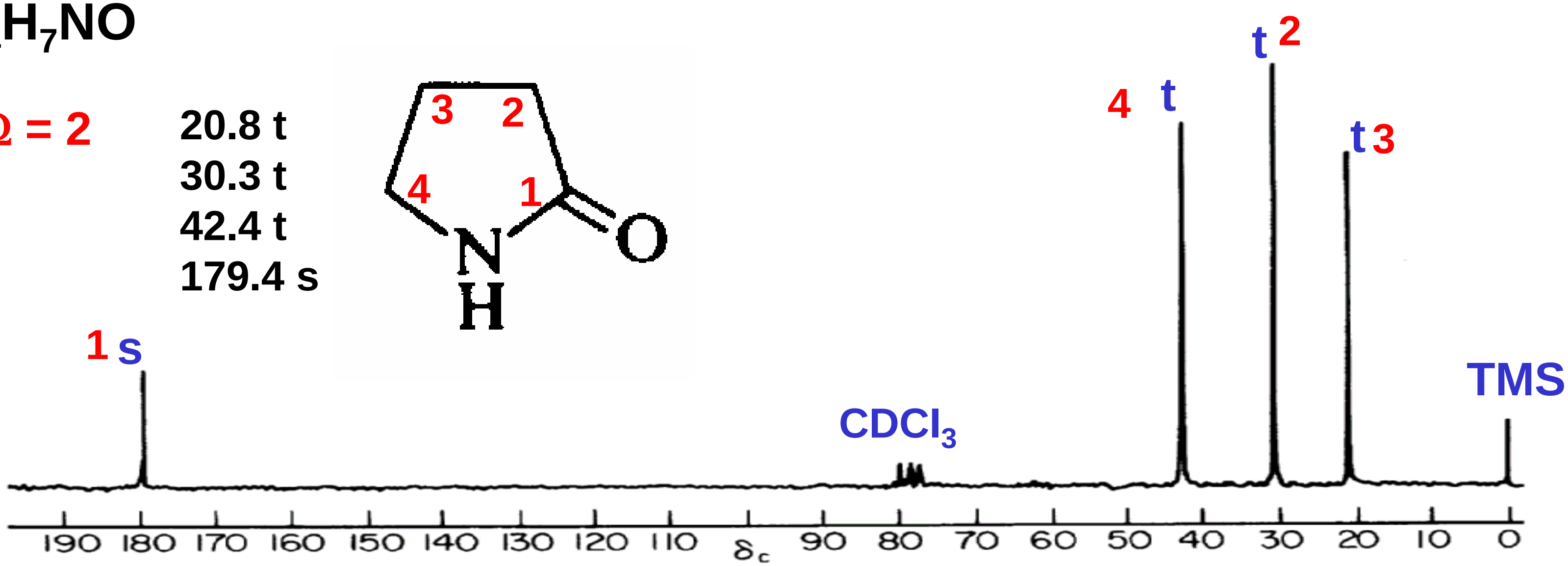


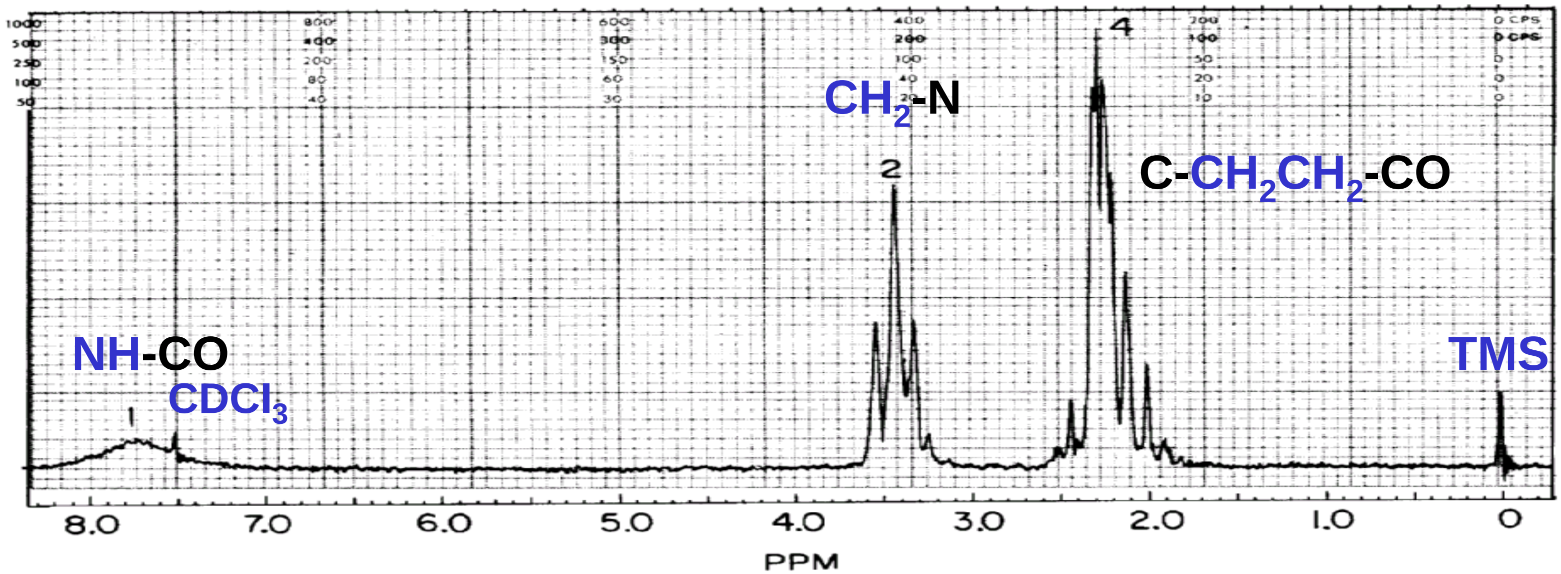


C_4H_7NO

$\Omega = 2$

20.8 t
30.3 t
42.4 t
179.4 s

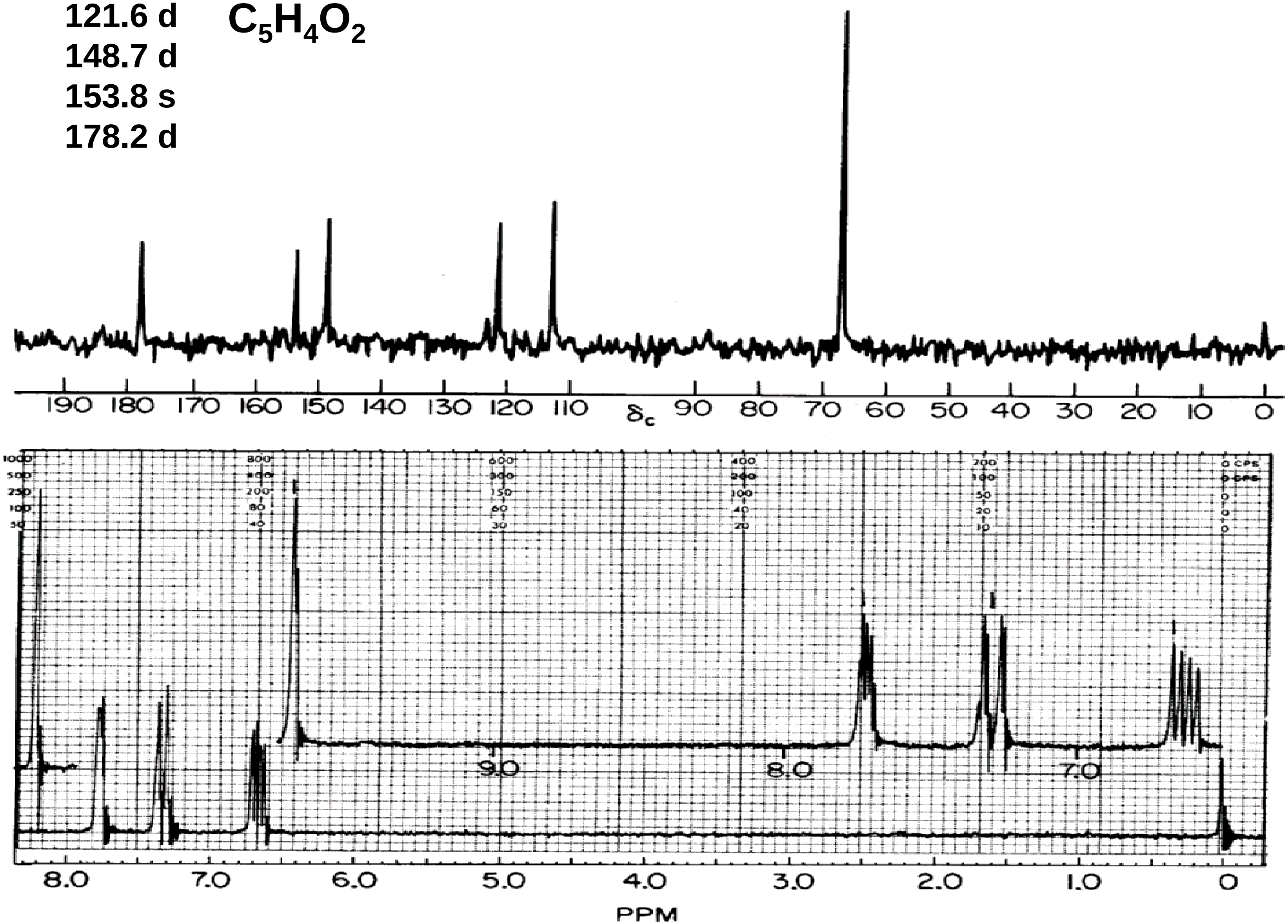




Problem 7

112.9 d
121.6 d
148.7 d
153.8 s
178.2 d

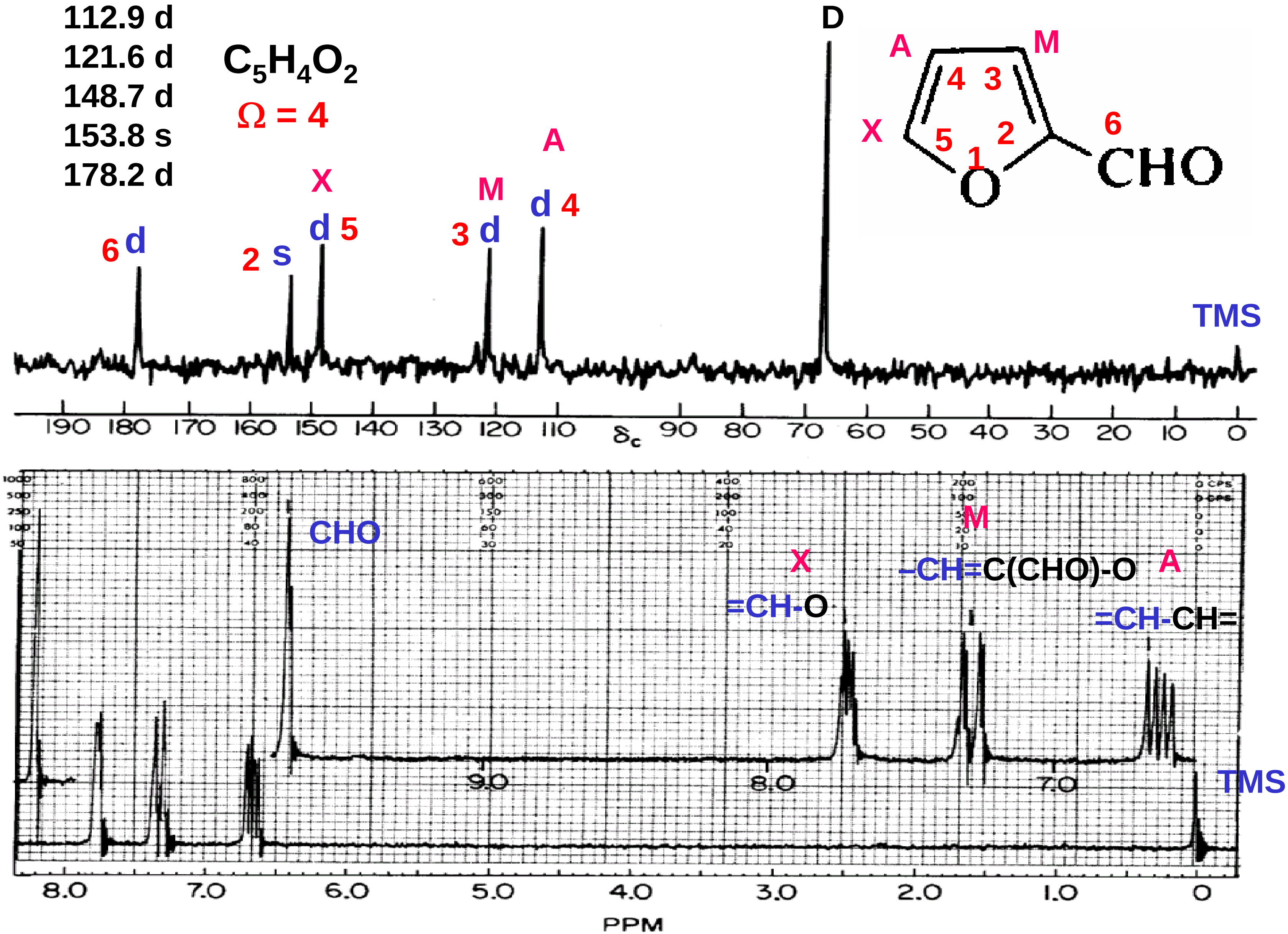
$C_5H_4O_2$



112.9 d
121.6 d
148.7 d
153.8 s
178.2 d

$C_5H_4O_2$

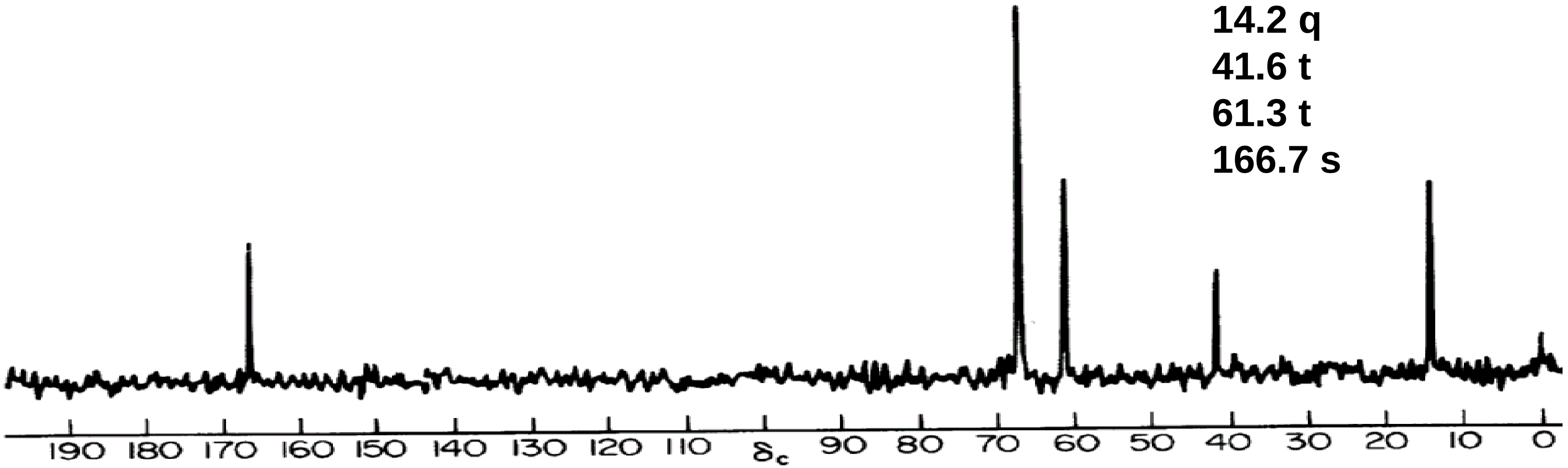
$\Omega = 4$

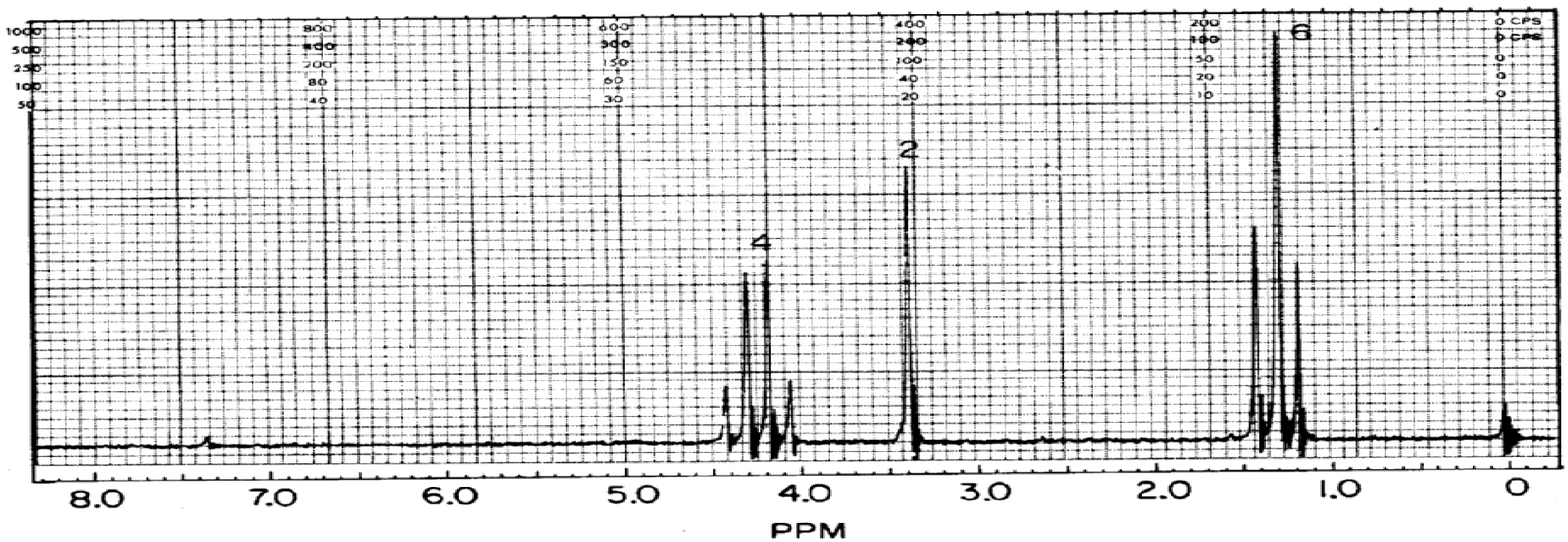


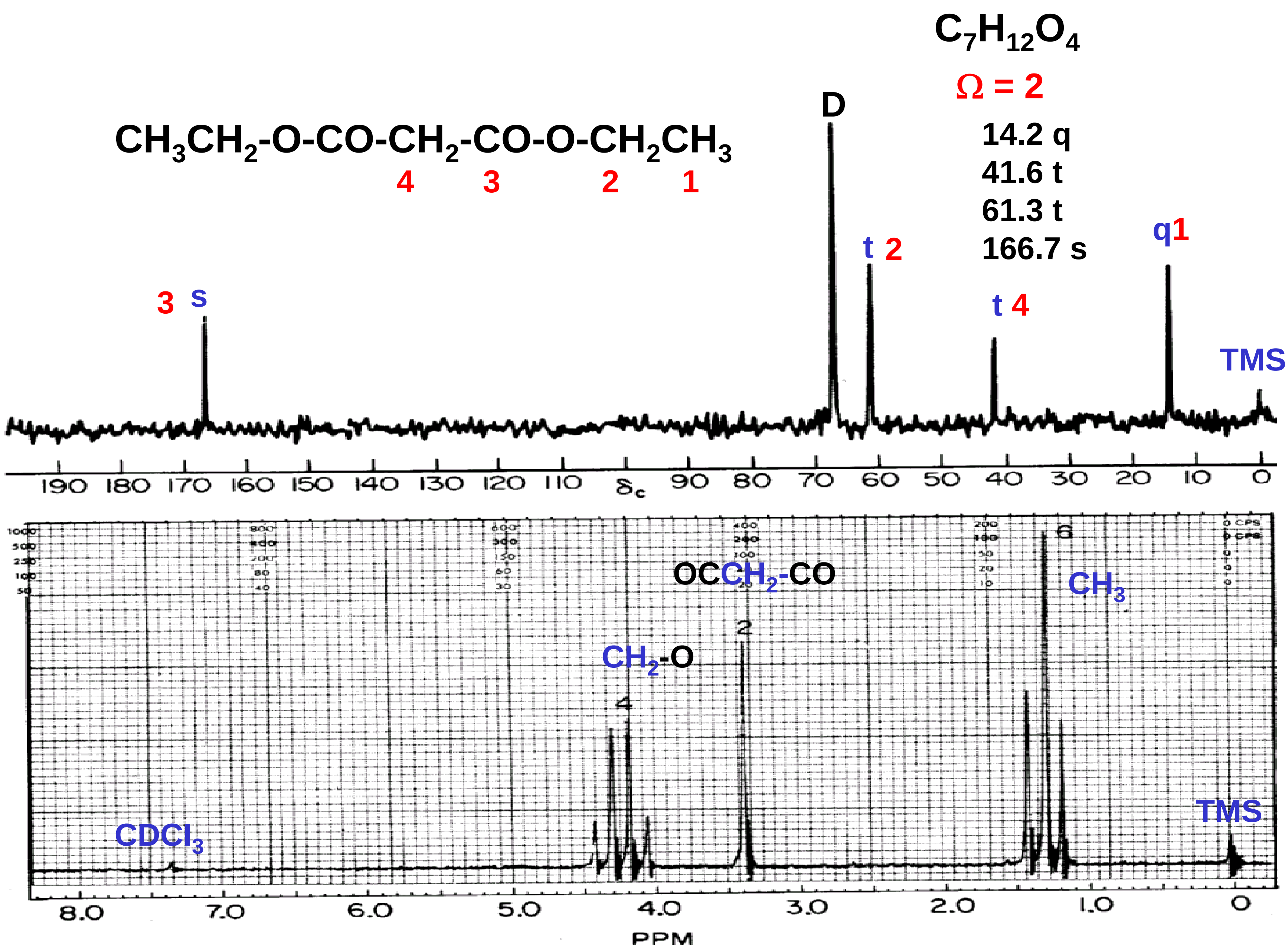
Problem 8

$C_7H_{12}O_4$

14.2 q
41.6 t
61.3 t
166.7 s





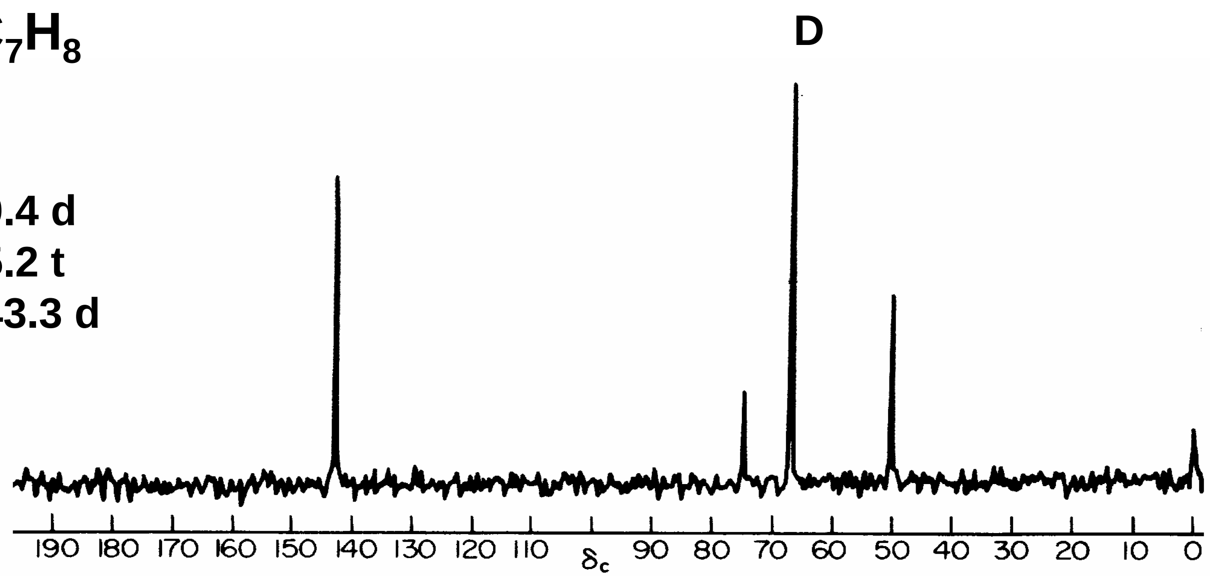


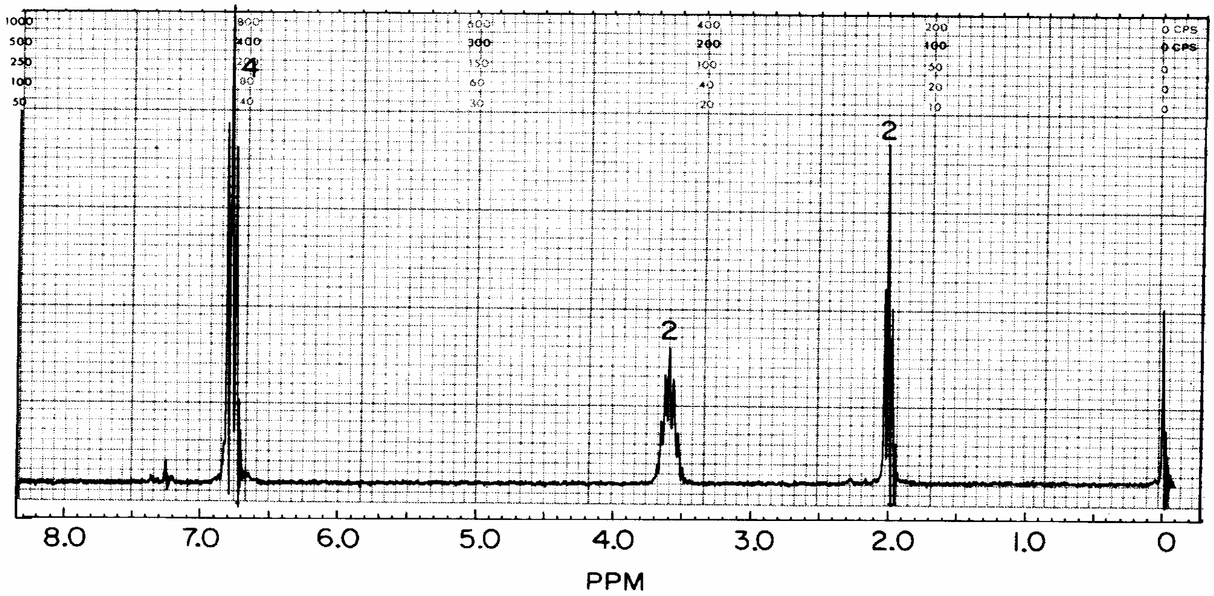
$C_7H_{12}O_4$
Ω = 2
CH_3CH_2-O-CO-CH_2-CO-O-CH_2CH_3
4 3 2 1
D
14.2 q
41.6 t
61.3 t
166.7 s
3 s
t 2
t 4
q1
TMS
190 180 170 160 150 140 130 120 110 δc 90 80 70 60 50 40 30 20 10 0
OCCH_2-CO
2
CH_3
6
CH_2-O
4
$CDCl_3$
TMS
8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
PPM

Problem 9

C_7H_8

50.4 d
75.2 t
143.3 d

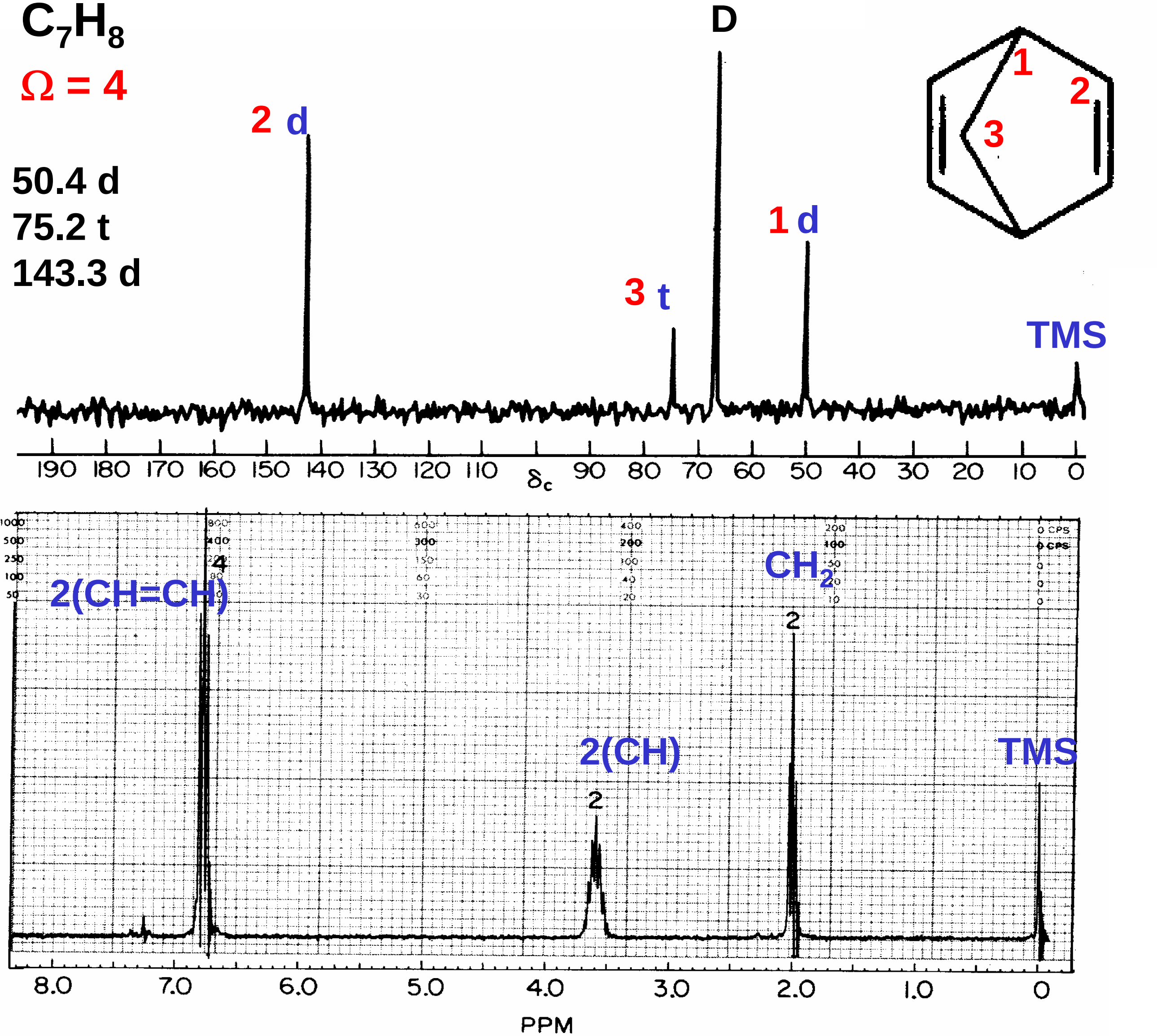




C_7H_8

$\Omega = 4$

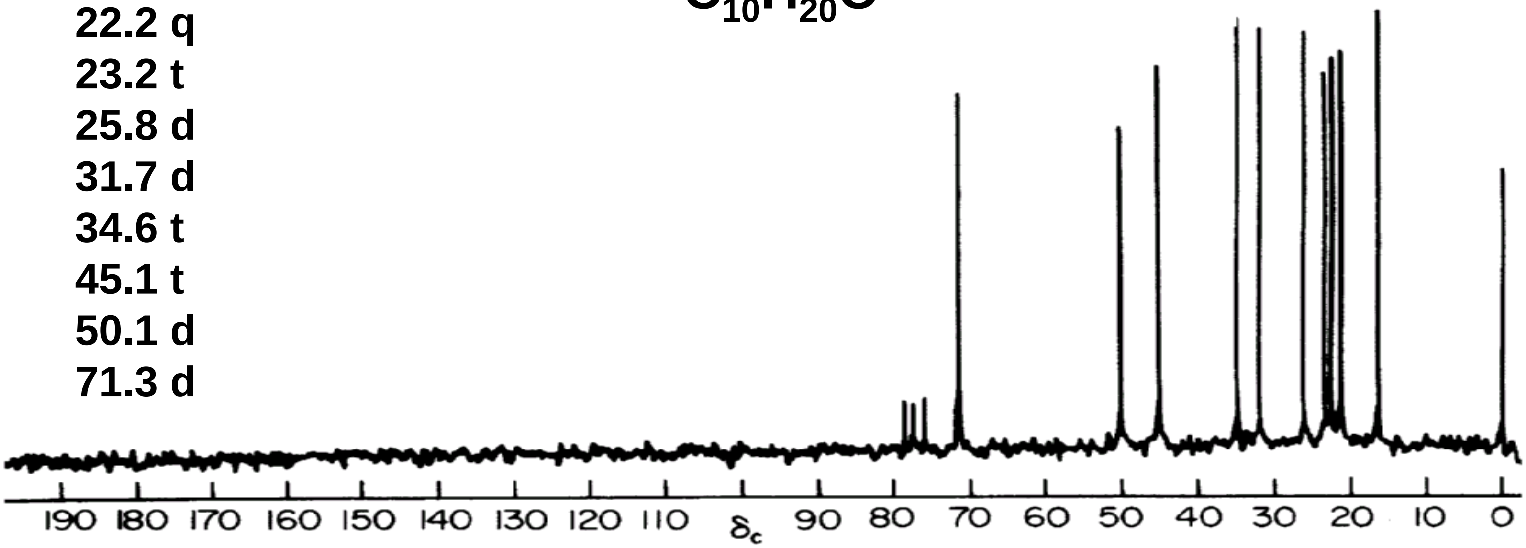
50.4 d
75.2 t
143.3 d

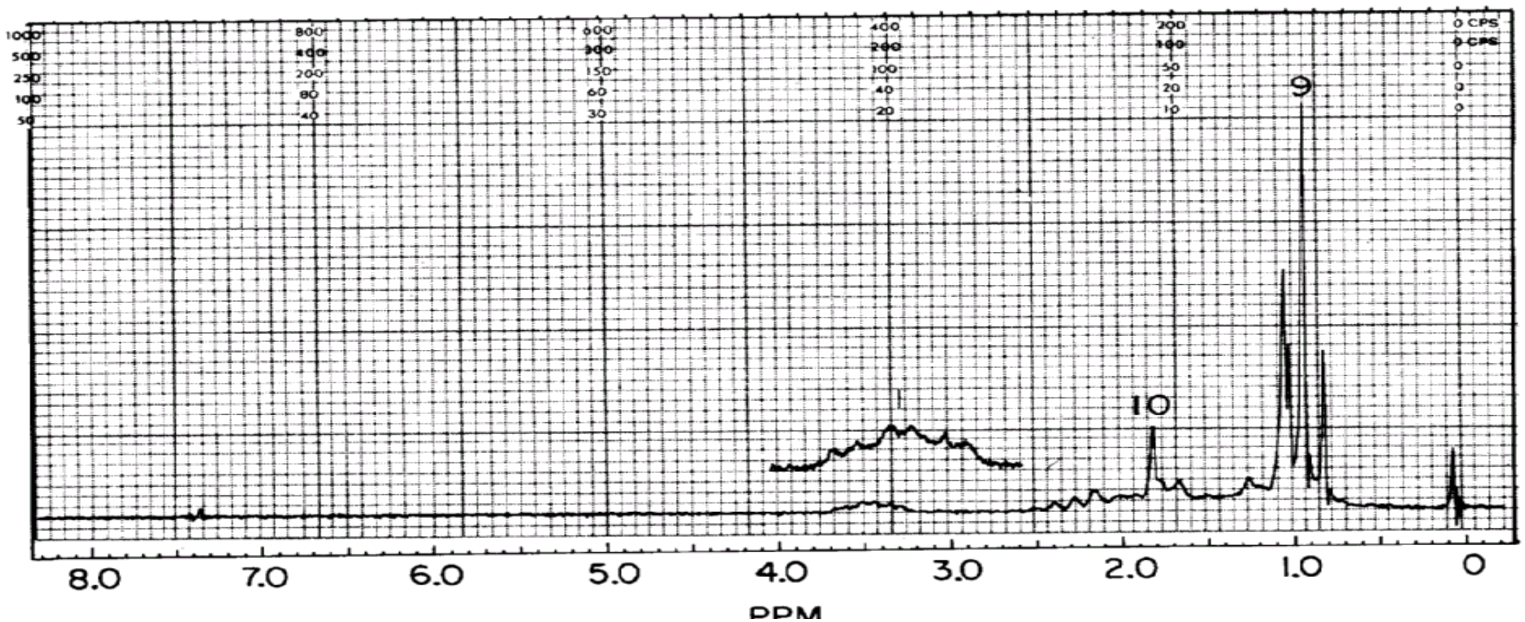


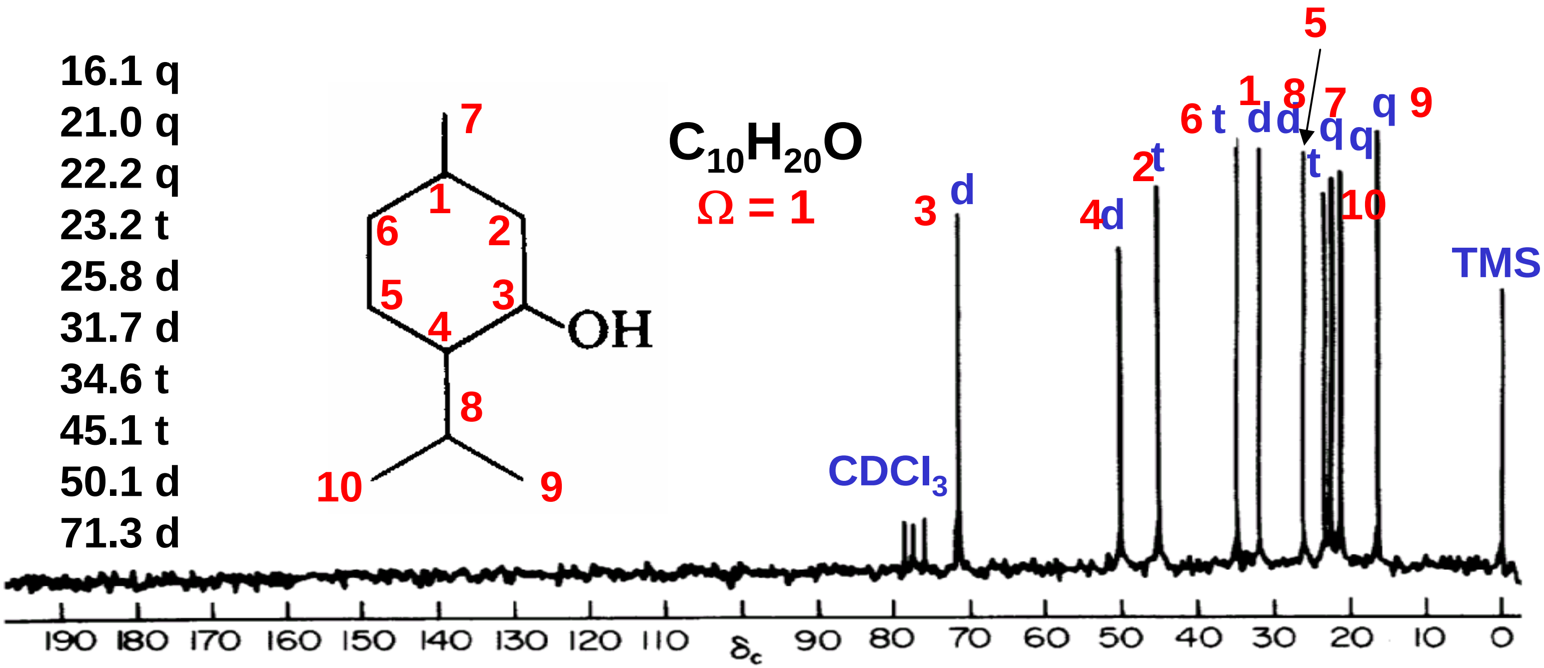
Problem 10

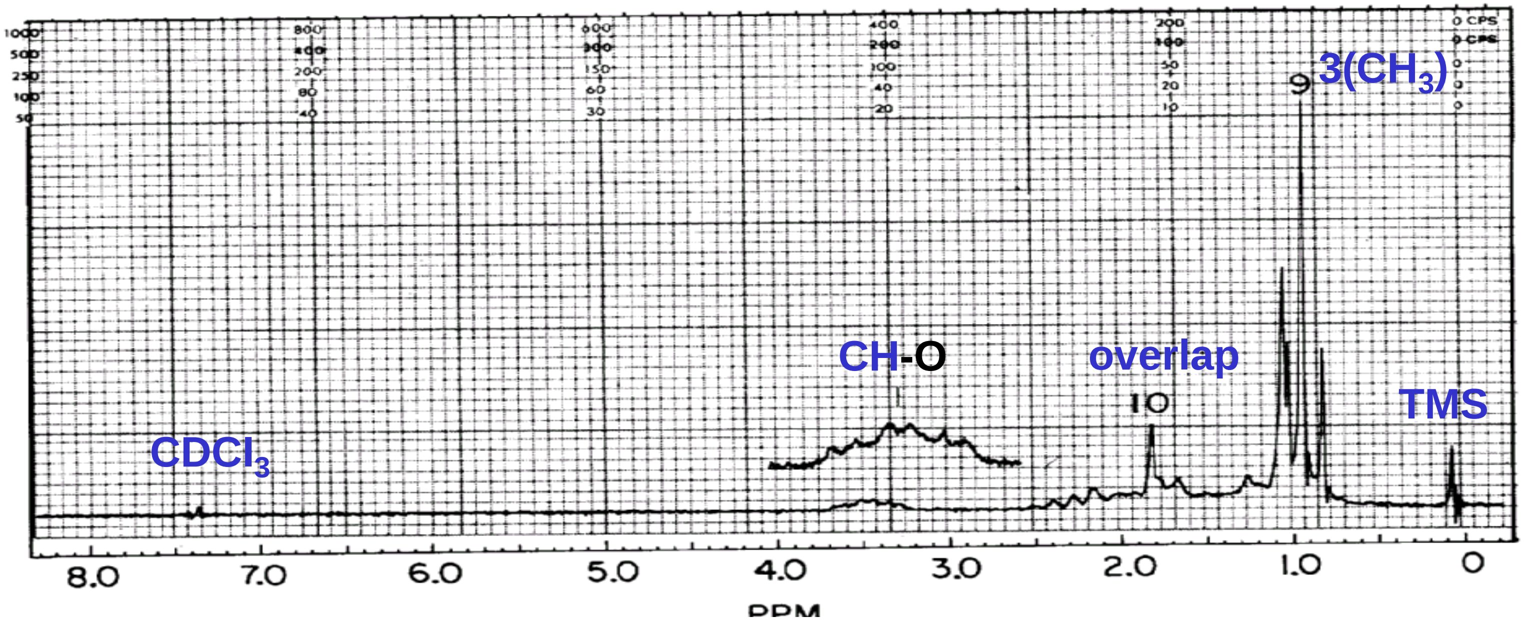
16.1 q
21.0 q
22.2 q
23.2 t
25.8 d
31.7 d
34.6 t
45.1 t
50.1 d
71.3 d

$C_{10}H_{20}O$





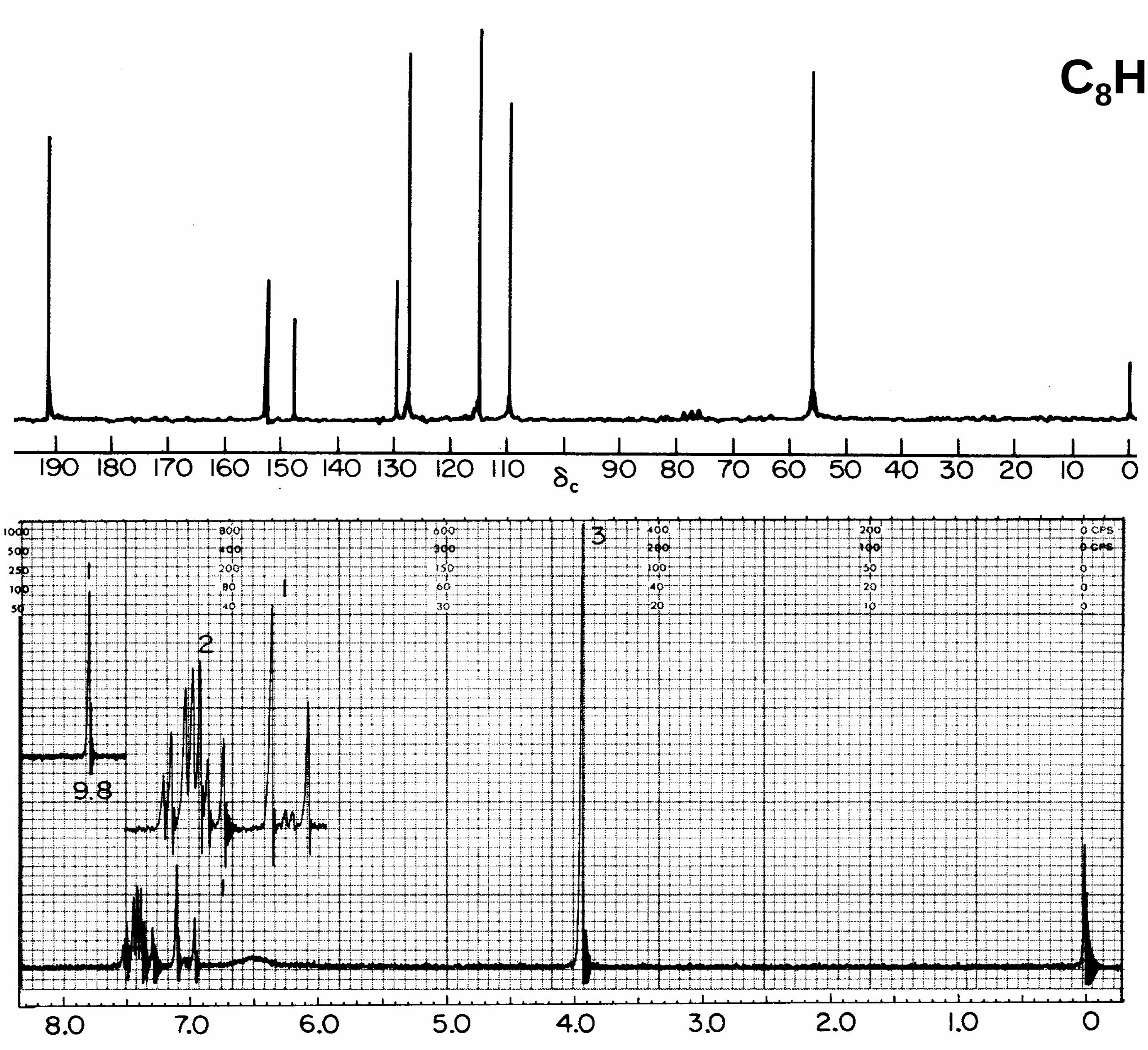

16.1 q
21.0 q
22.2 q
23.2 t
25.8 d
31.7 d
34.6 t
45.1 t
50.1 d
71.3 d
7
1
2
3
4
5
6
8
9
10
OH
C10H20O
Ω = 1
3 d
4d
2 t
6 t
1 d
8 d
5
t
7 q
q
q 9
10
TMS
CDCl3
190 180 170 160 150 140 130 120 110 δc 90 80 70 60 50 40 30 20 10 0


9
3(CH3)
CH-O
overlap
10
TMS
CDCl3
8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
PPM

Problem 11

56.0 q
109.4 d
114.8 d
127.4 d
129.5 s
147.5 s
152.3 s
191.3 d

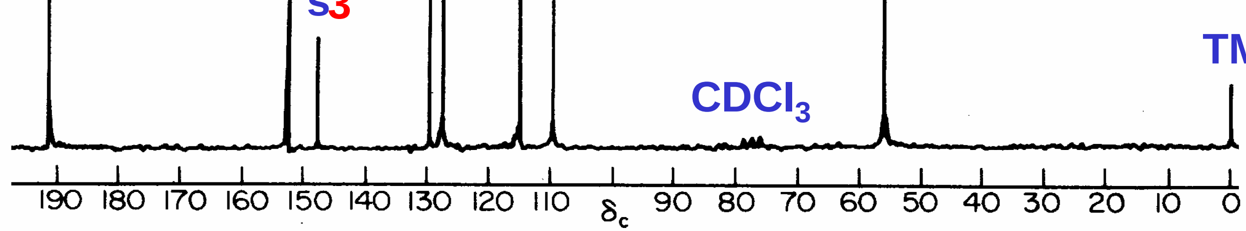
$C_8H_8O_3$

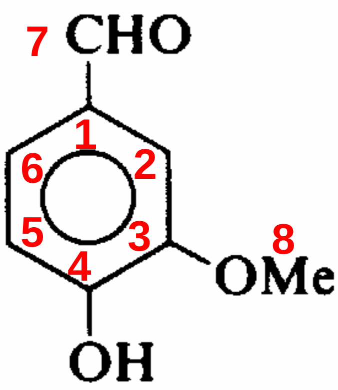


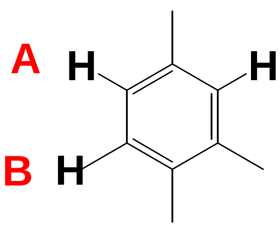
56.0 q
109.4 d
114.8 d
127.4 d
129.5 s
147.5 s
152.3 s
191.3 d

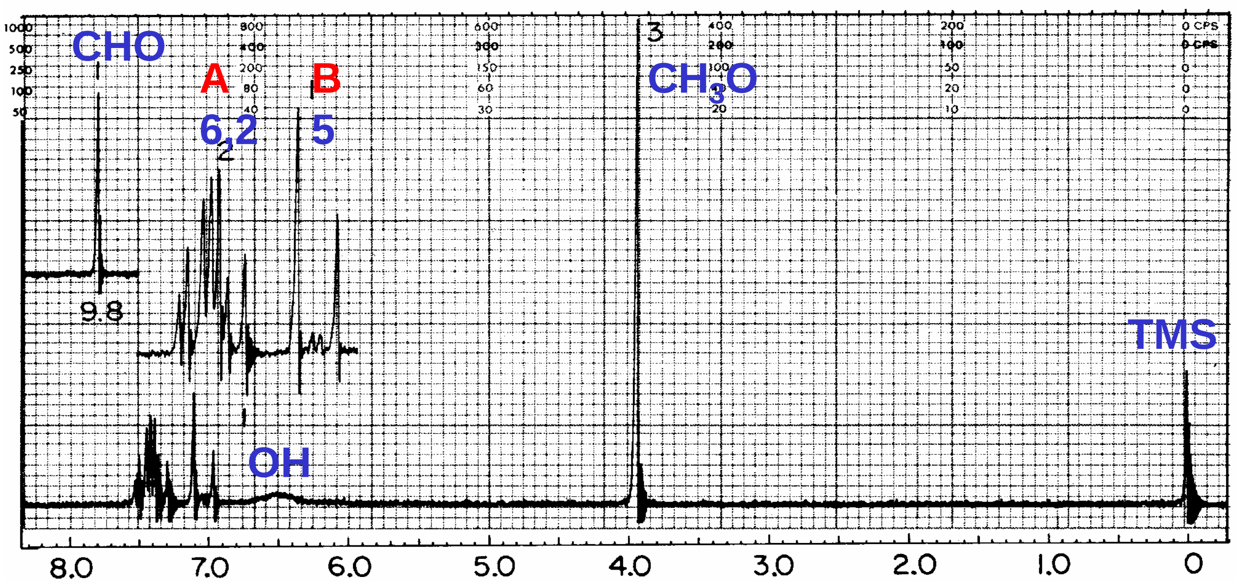
$C_8H_8O_3$

$\Omega = 5$





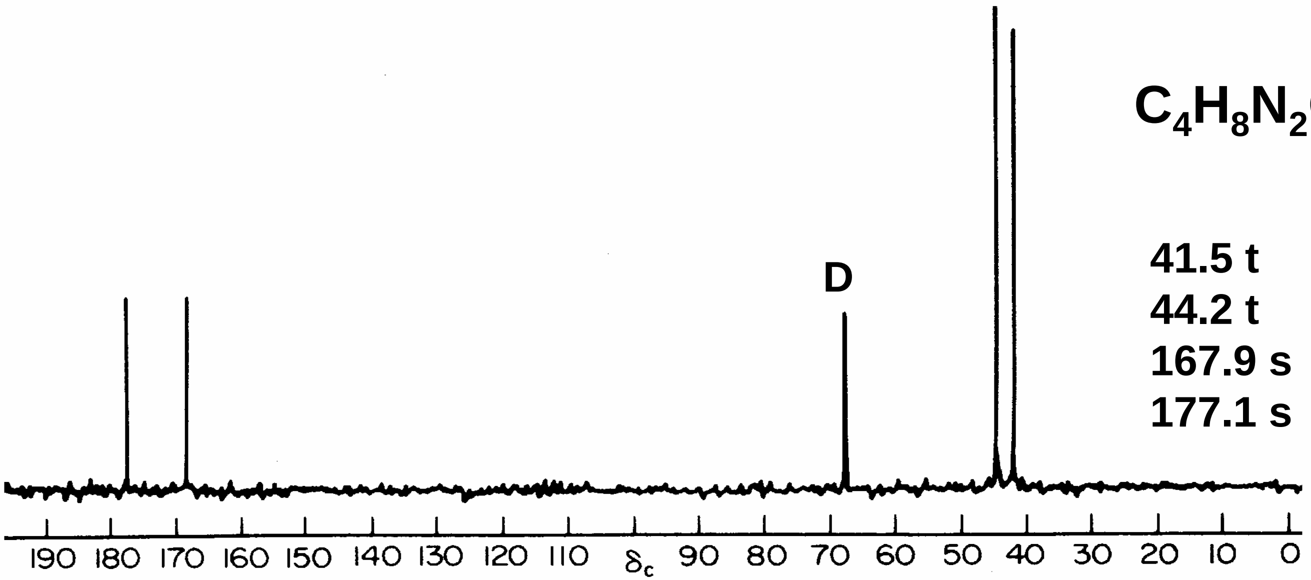


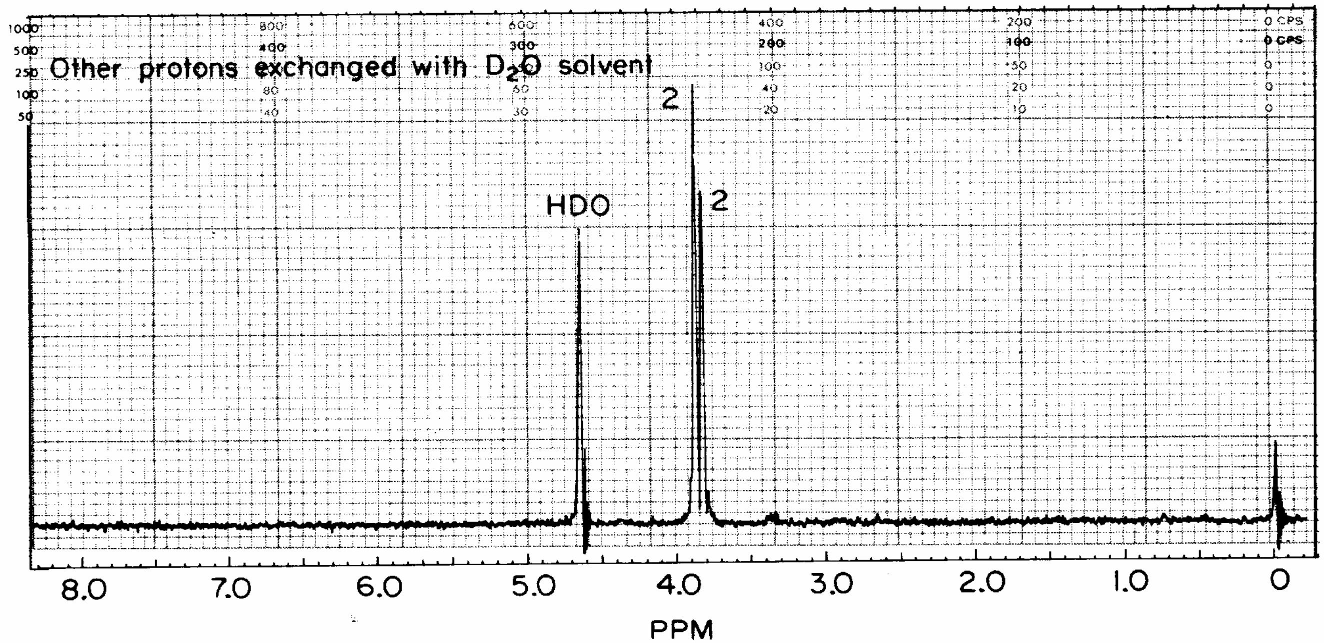


Problem 12

$C_4H_8N_2O_3$

41.5 t
44.2 t
167.9 s
177.1 s



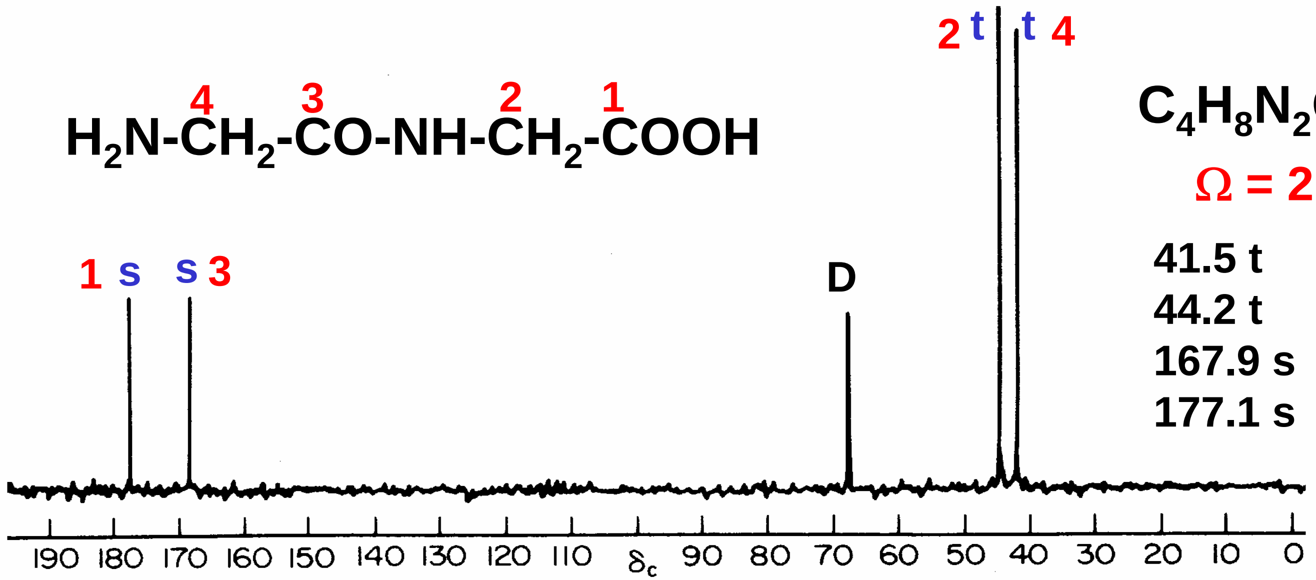


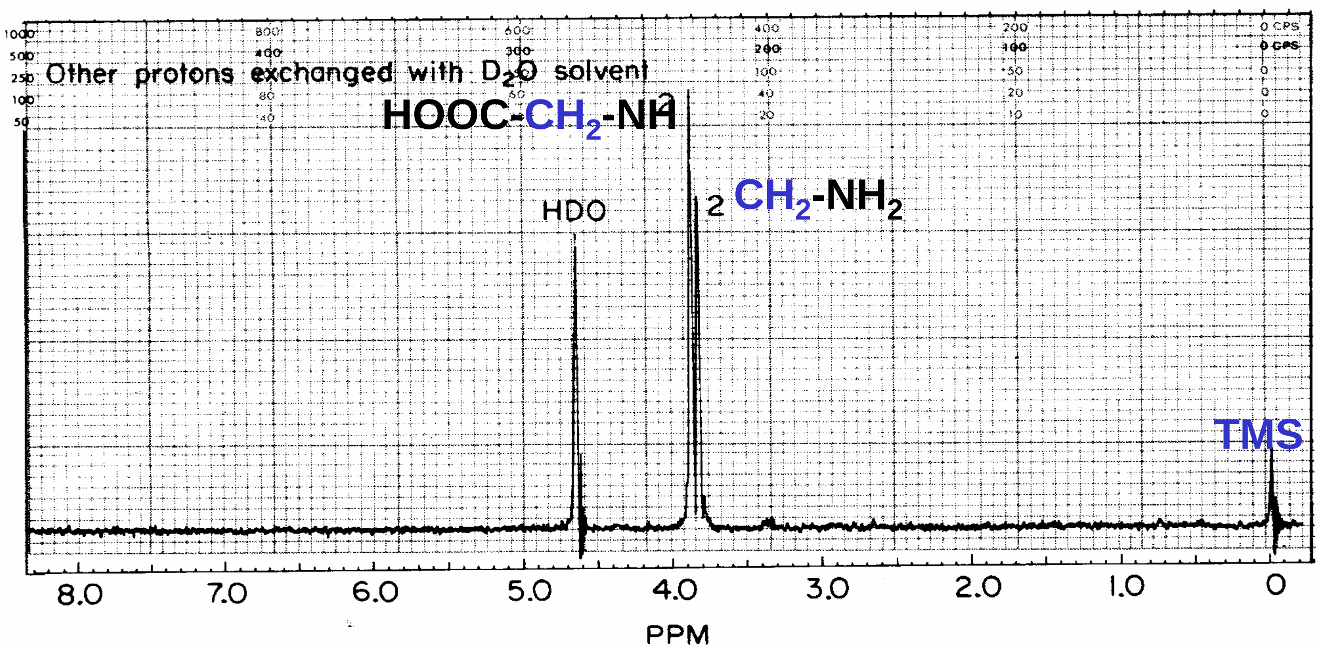
$H_2N-CH_2-CO-NH-CH_2-COOH$ (carbons numbered 4, 3, 2, 1)

$C_4H_8N_2O_3$

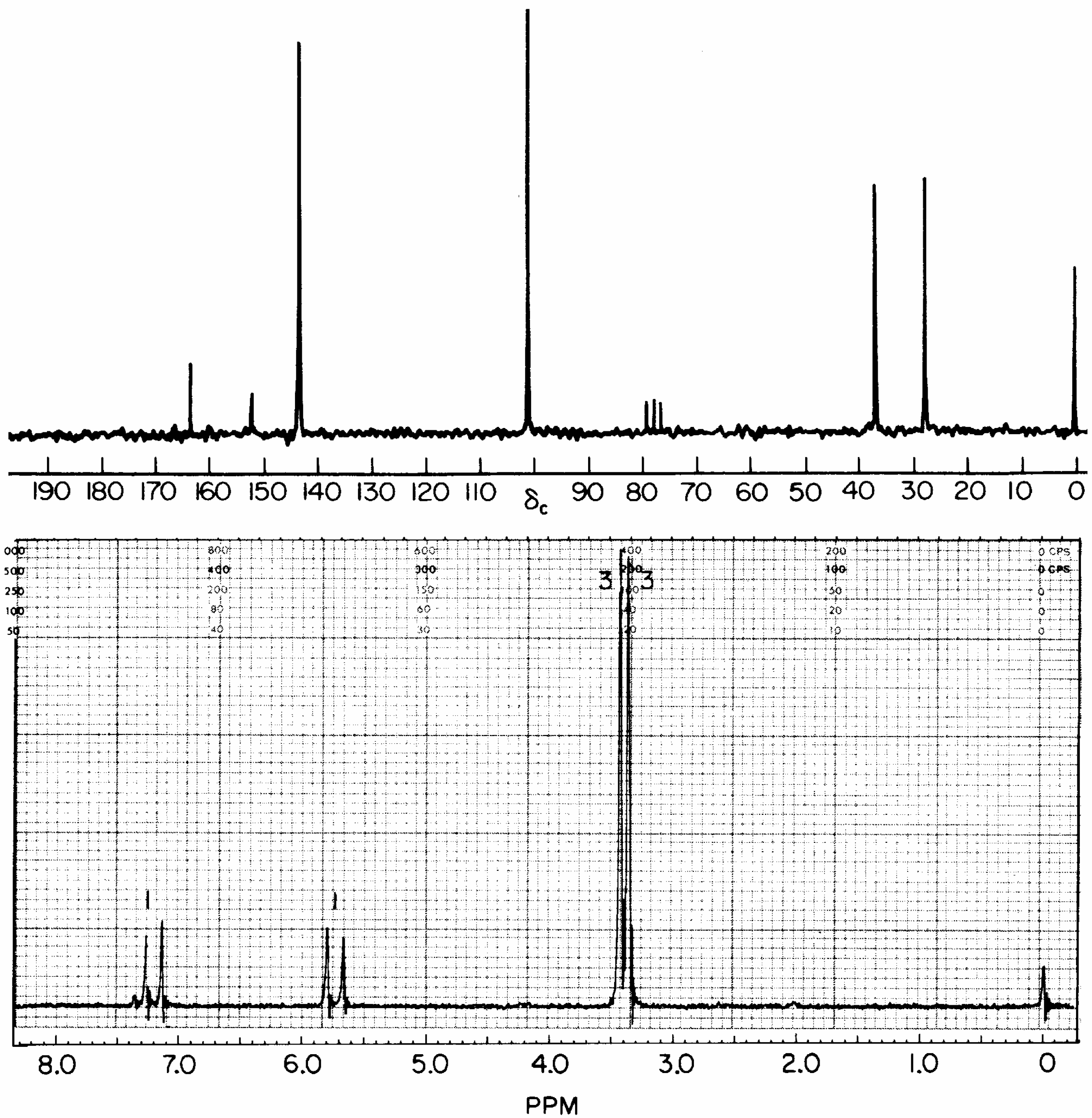
$\Omega = 2$

41.5 t
44.2 t
167.9 s
177.1 s





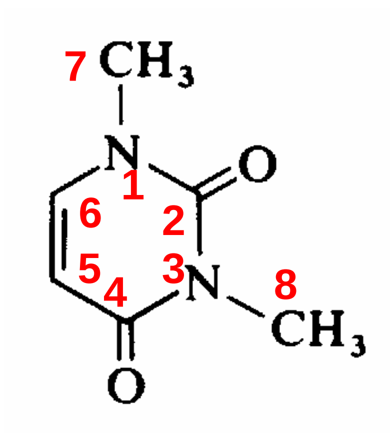
Problem 13

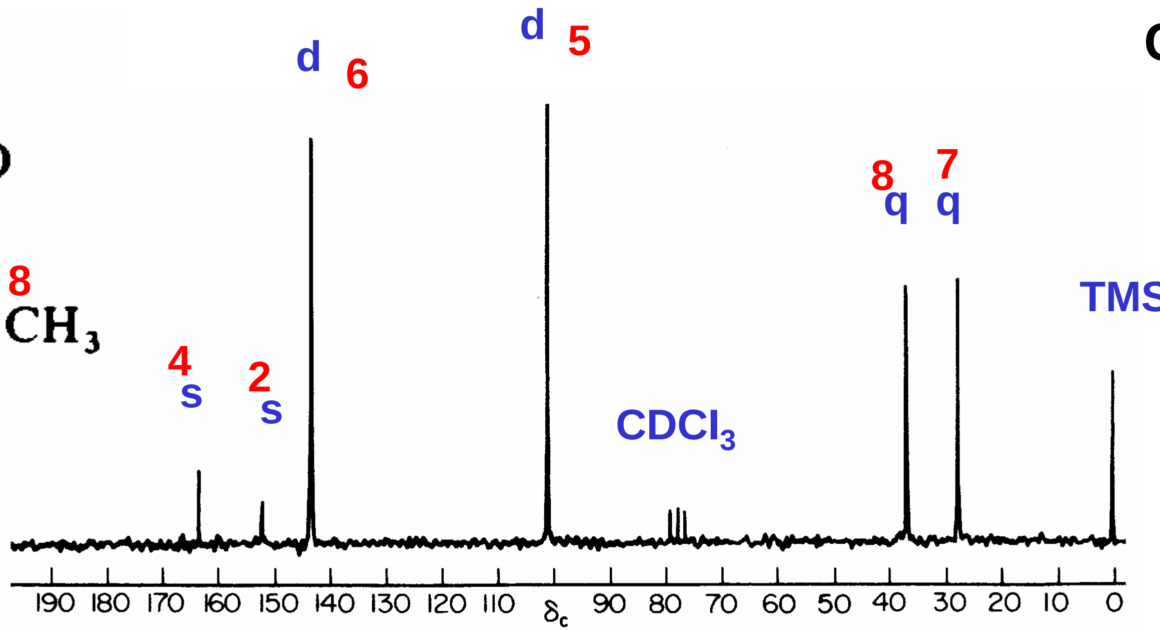


$C_6H_8N_2O_2$

$\Omega = 4$

27.5 q
36.8 q
100.9 d
143.2 d
151.8 s
163.2 s

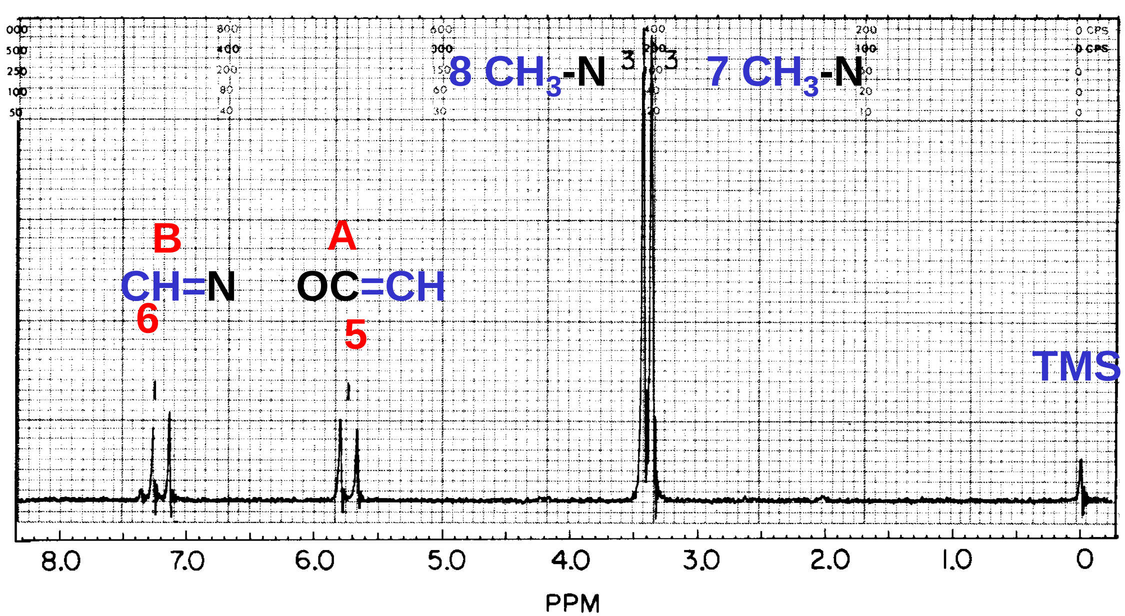




$C_6H_8N_2O_2$

$\Omega = 4$

27.5 q
36 8 q
100.9 d
143.2 d
151.8 s
163.2 s

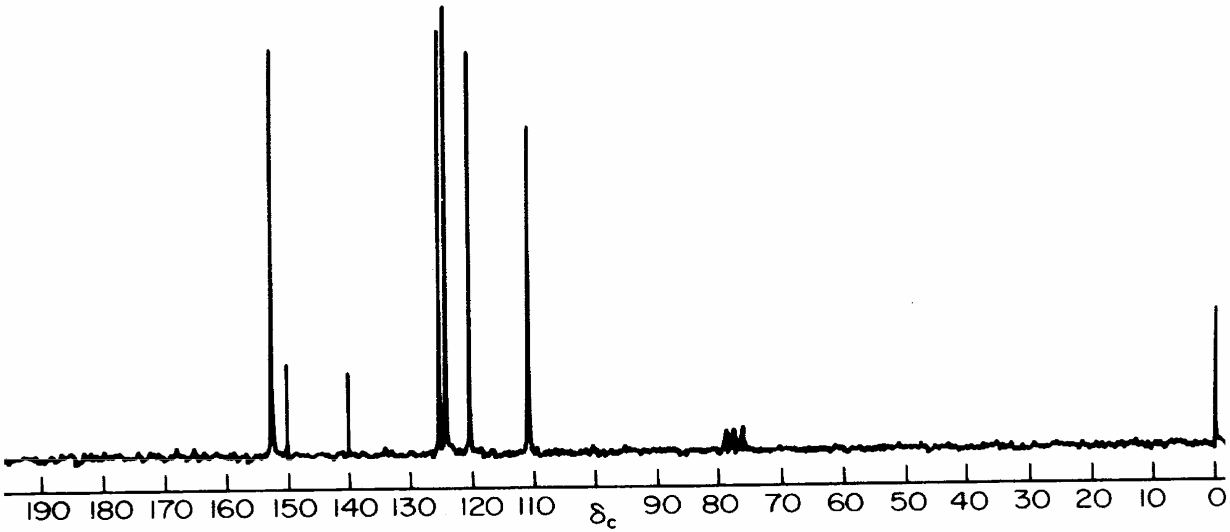


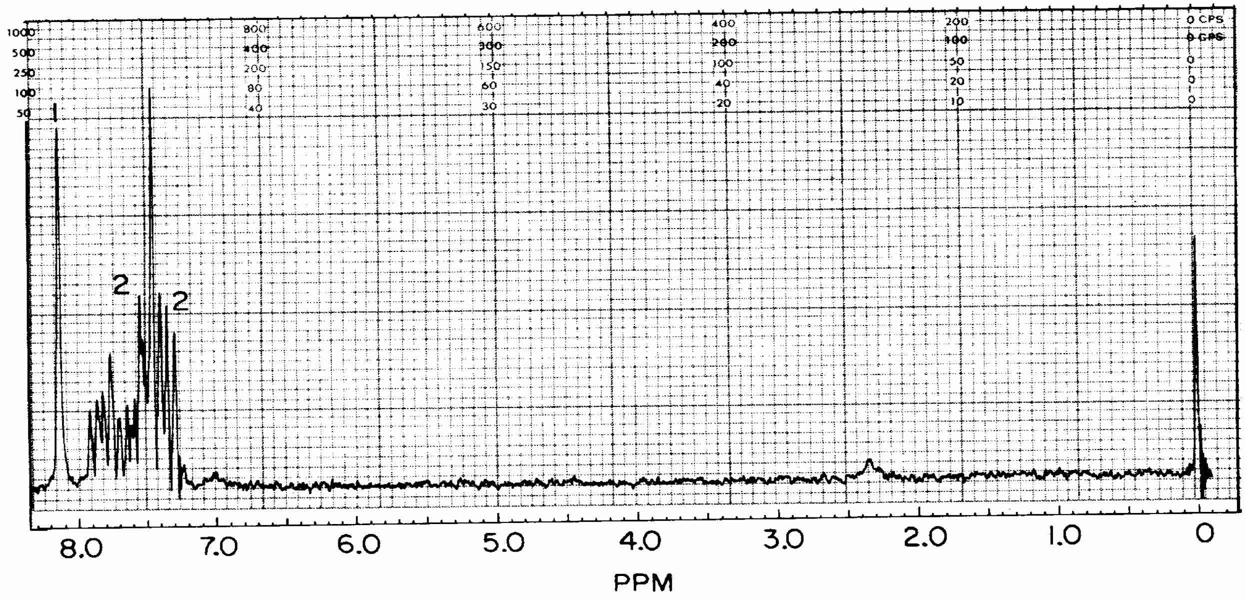
Problem 14

C_7H_5NO

$\Omega = 6$

110.8 d
120.5 d
124.4 d
125.4 d
140.1 s
150.0 s
152.6 d

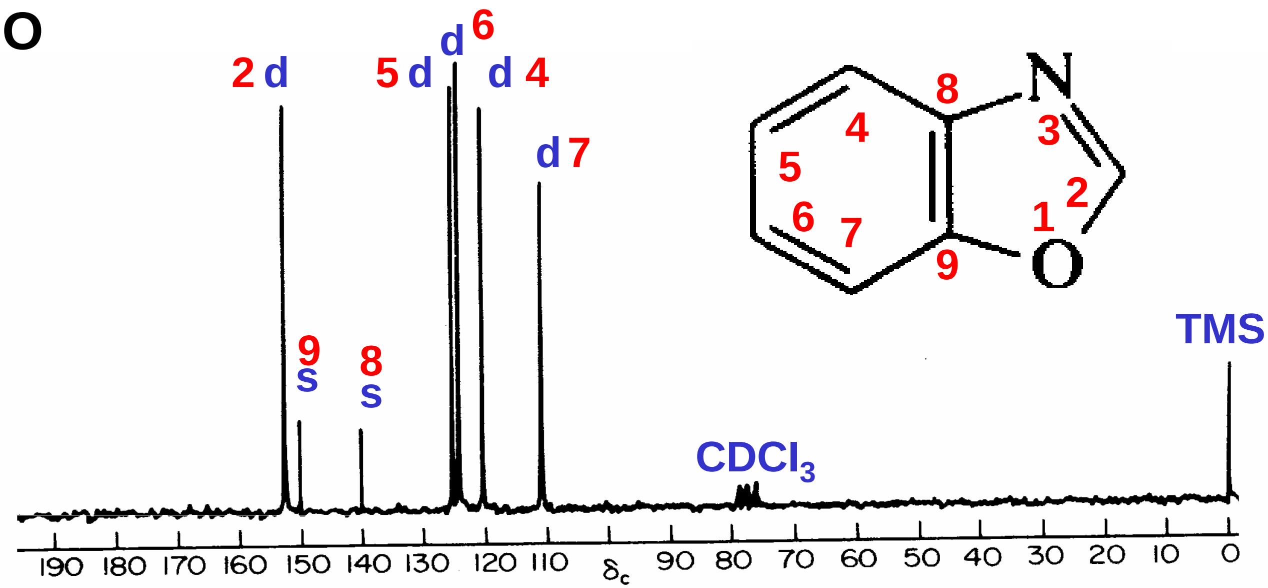


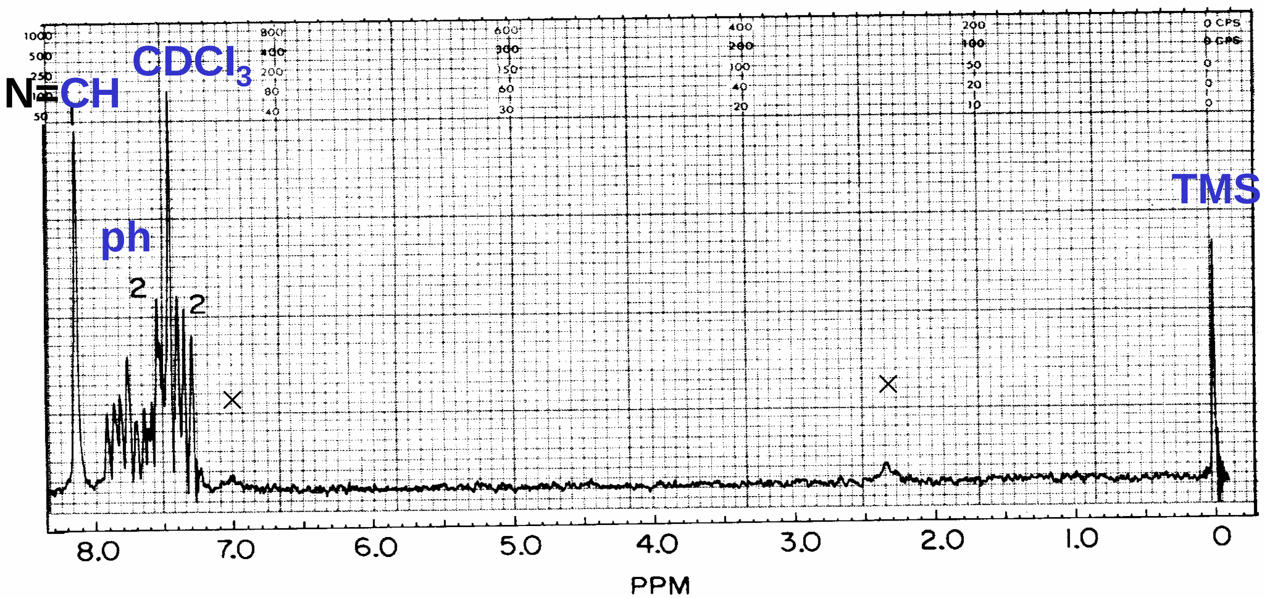


C_7H_5NO

$\Omega = 6$

110.8 d
120.5 d
124.4 d
125.4 d
140.1 s
150.0 s
152.6 d



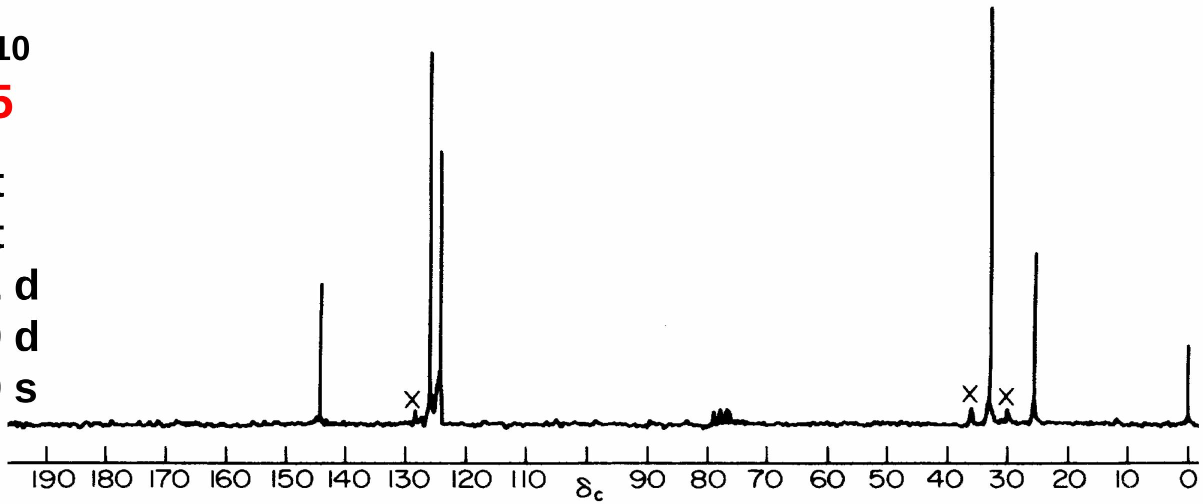


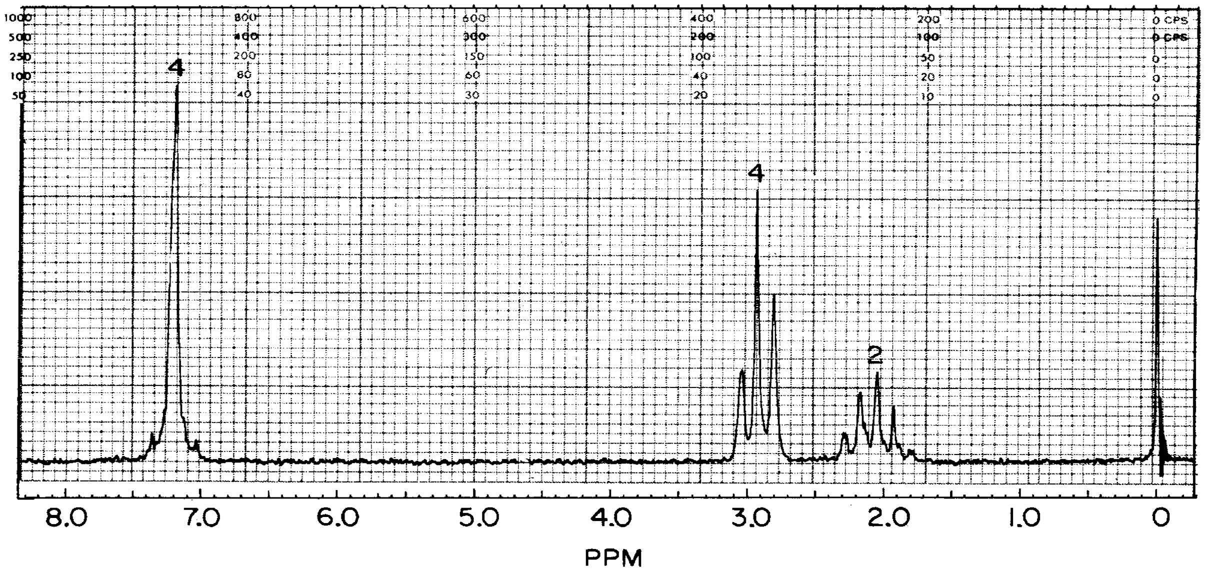
Problem 15

C_9H_{10}

$\Omega = 5$

25.3 t
32.8 t
124.2 d
125.9 d
143.9 s

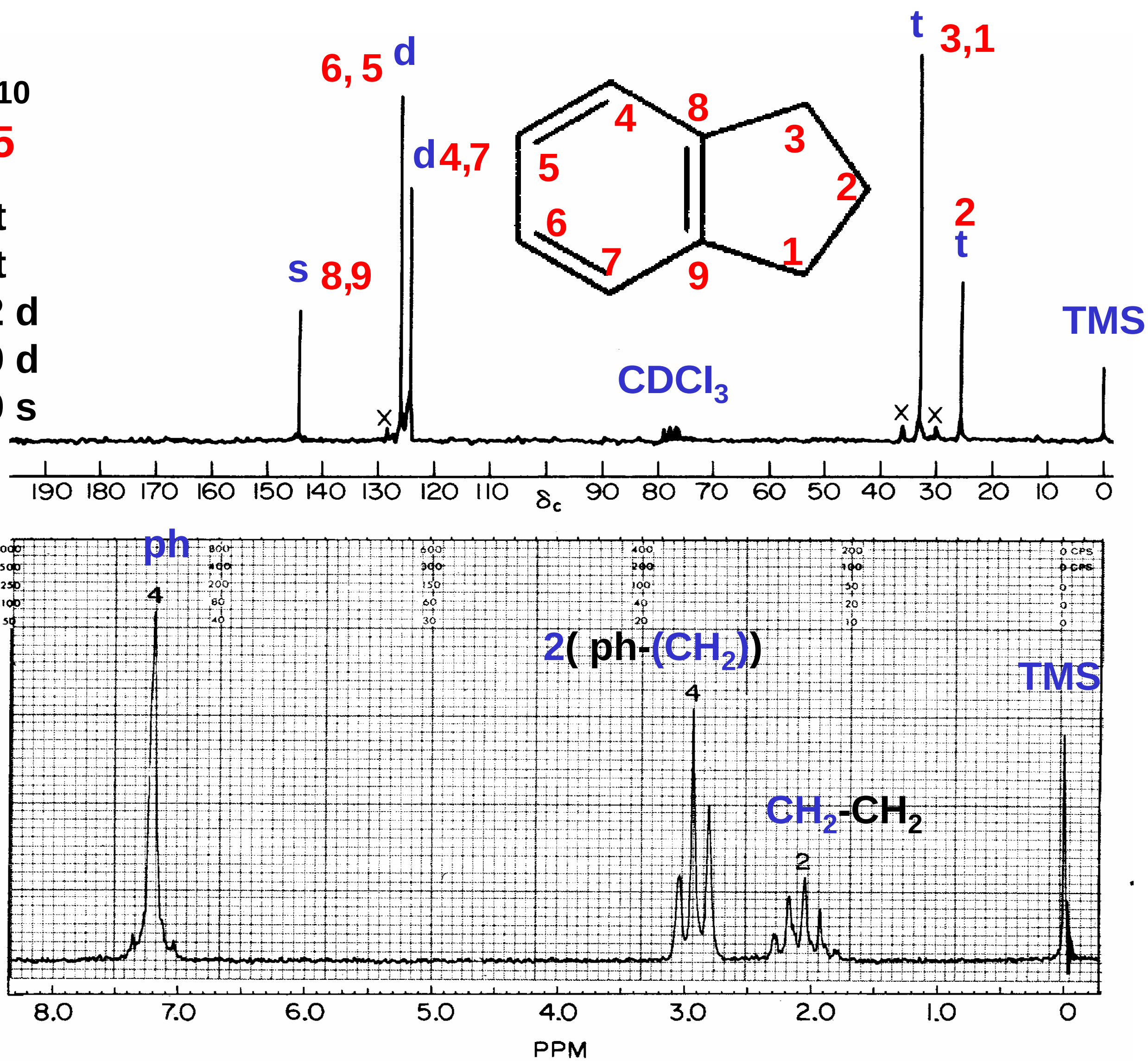




C_9H_{10}

$\Omega = 5$

25.3 t
32.8 t
124.2 d
125.9 d
143.9 s

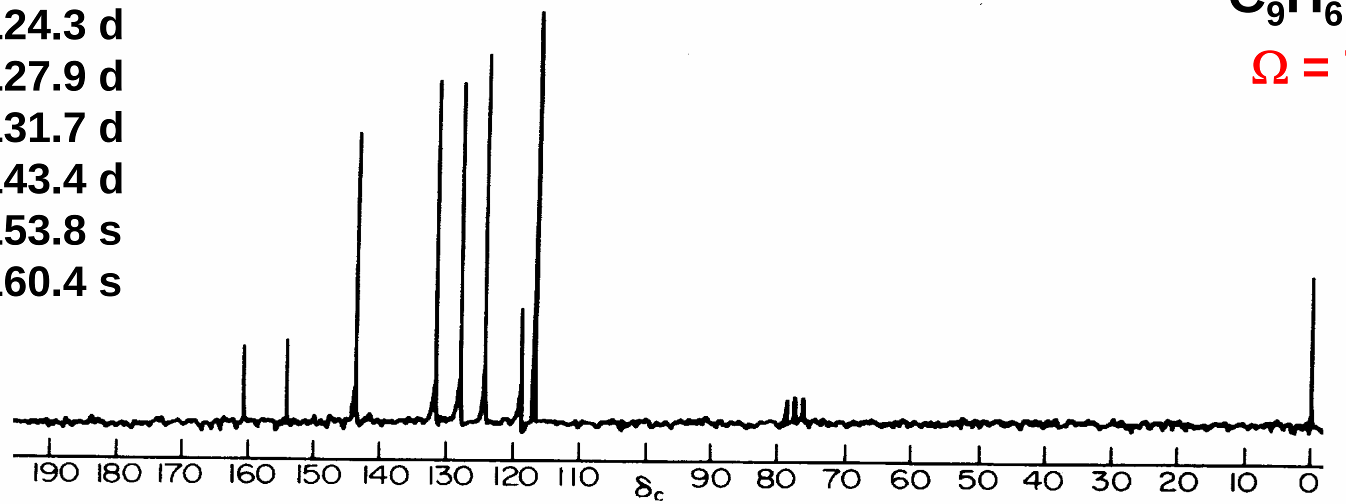


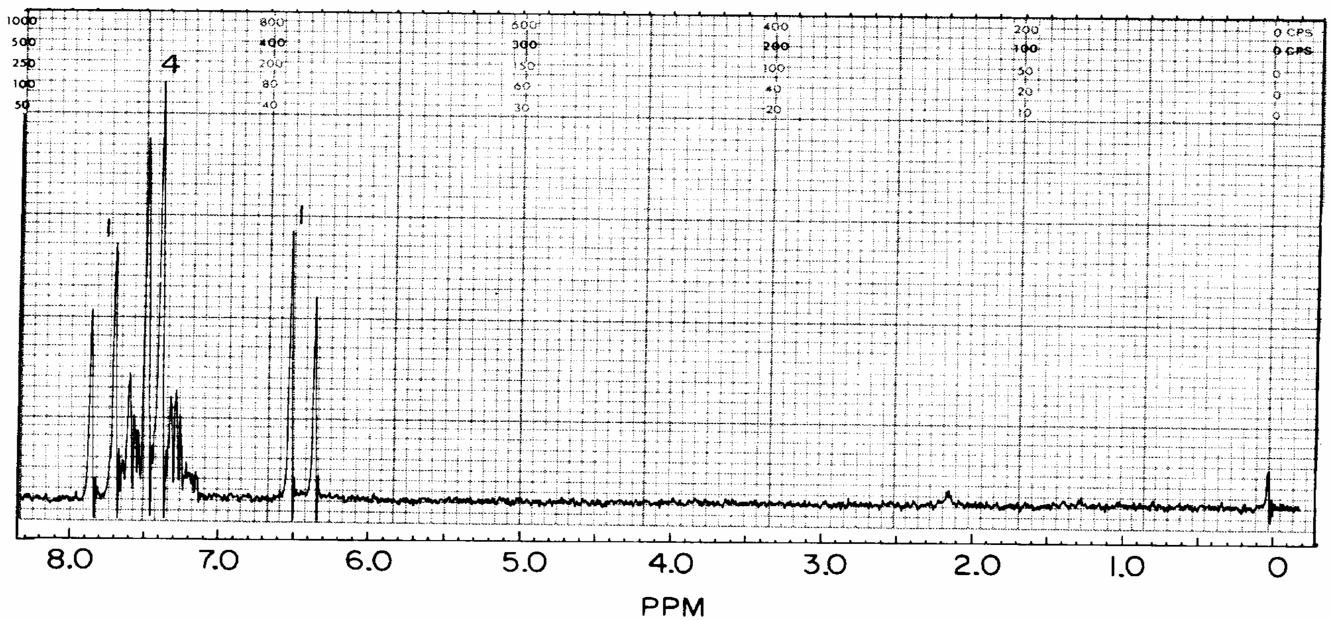
Problem 16

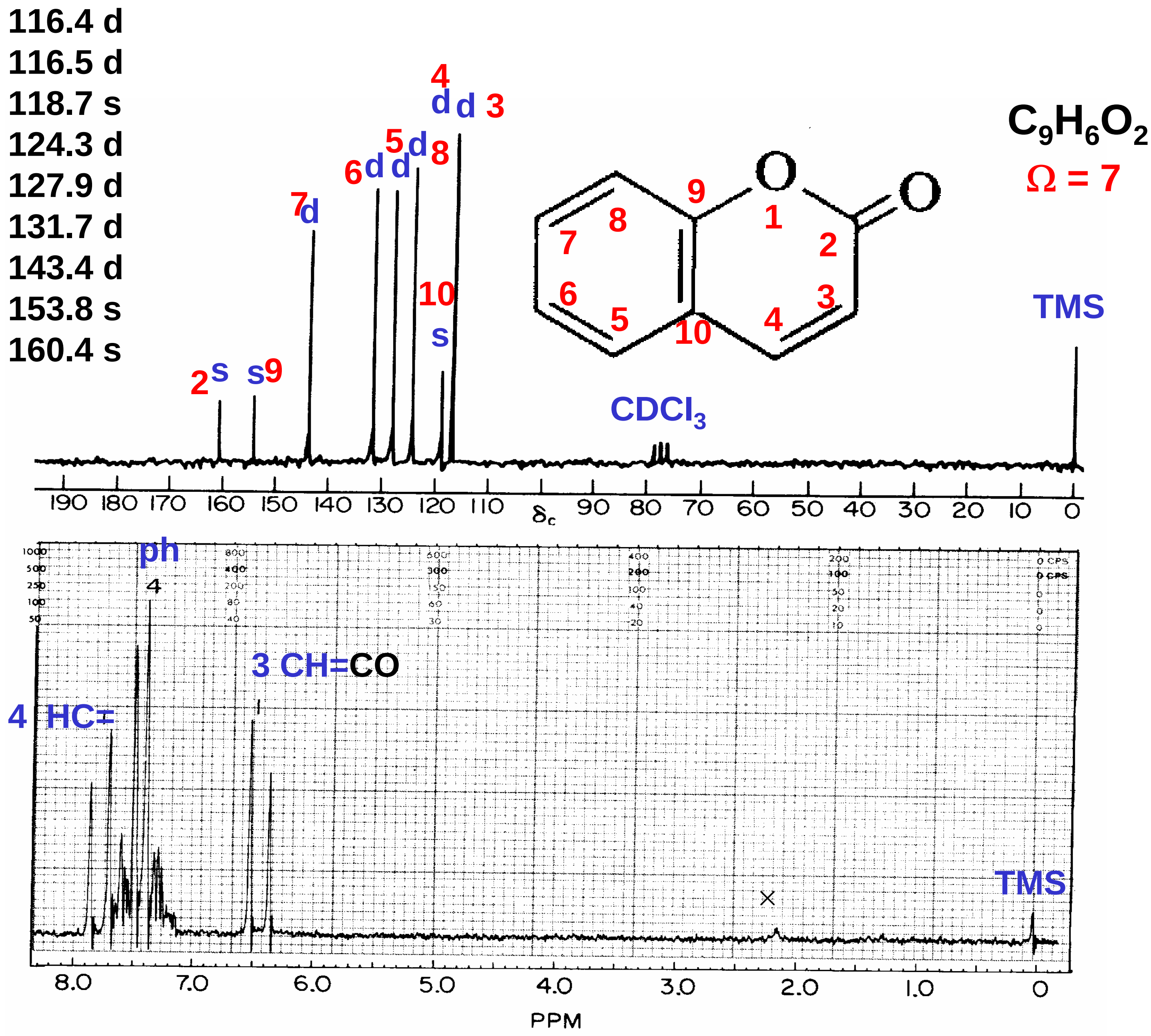
116.4 d
116.5 d
118.7 s
124.3 d
127.9 d
131.7 d
143.4 d
153.8 s
160.4 s

$C_9H_6O_2$

$\Omega = 7$







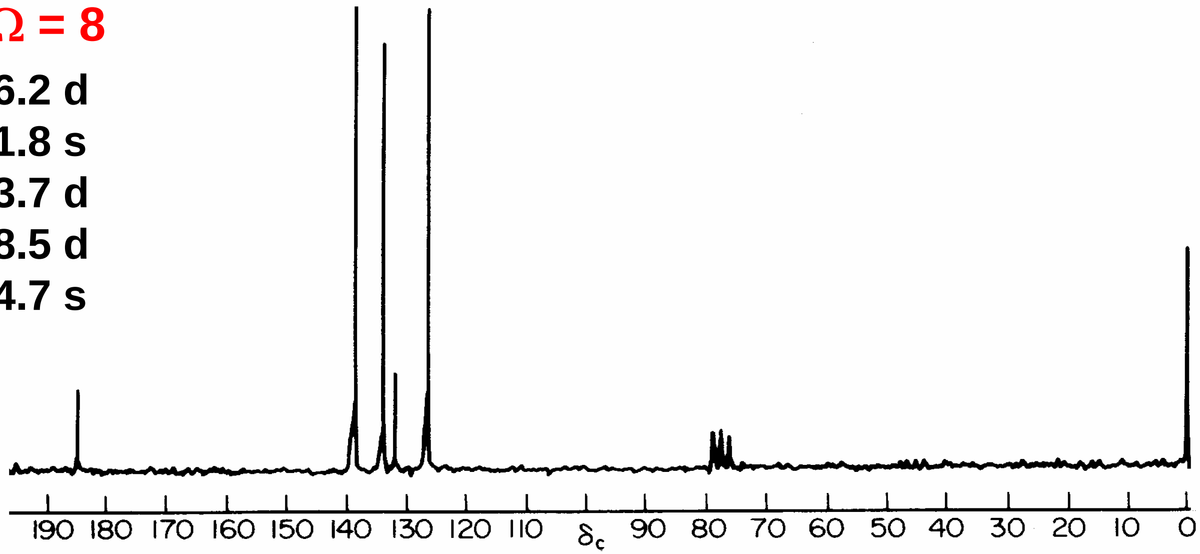
116.4 d
116.5 d
118.7 s
124.3 d
127.9 d
131.7 d
143.4 d
153.8 s
160.4 s
$C_9H_6O_2$
$\Omega = 7$
TMS
$CDCl_3$
δ_c
190 180 170 160 150 140 130 120 110 90 80 70 60 50 40 30 20 10 0
ph
4 HC=
3 CH=CO
TMS
8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
PPM

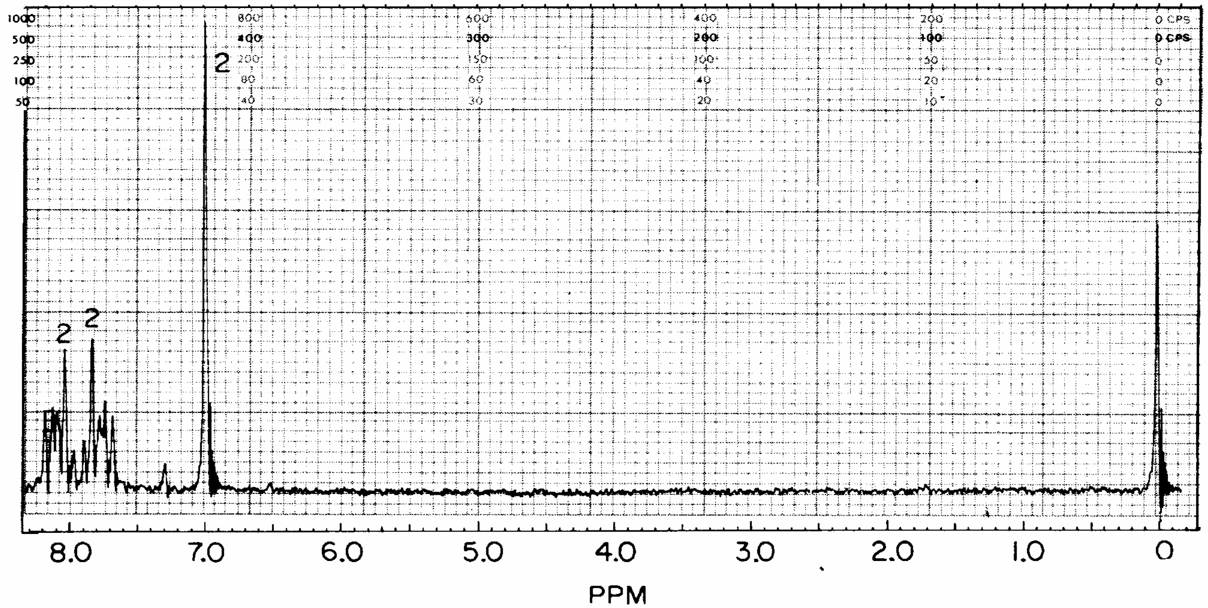
Problem 17

$C_{10}H_6O_2$

$\Omega = 8$

126.2 d
131.8 s
133.7 d
138.5 d
184.7 s

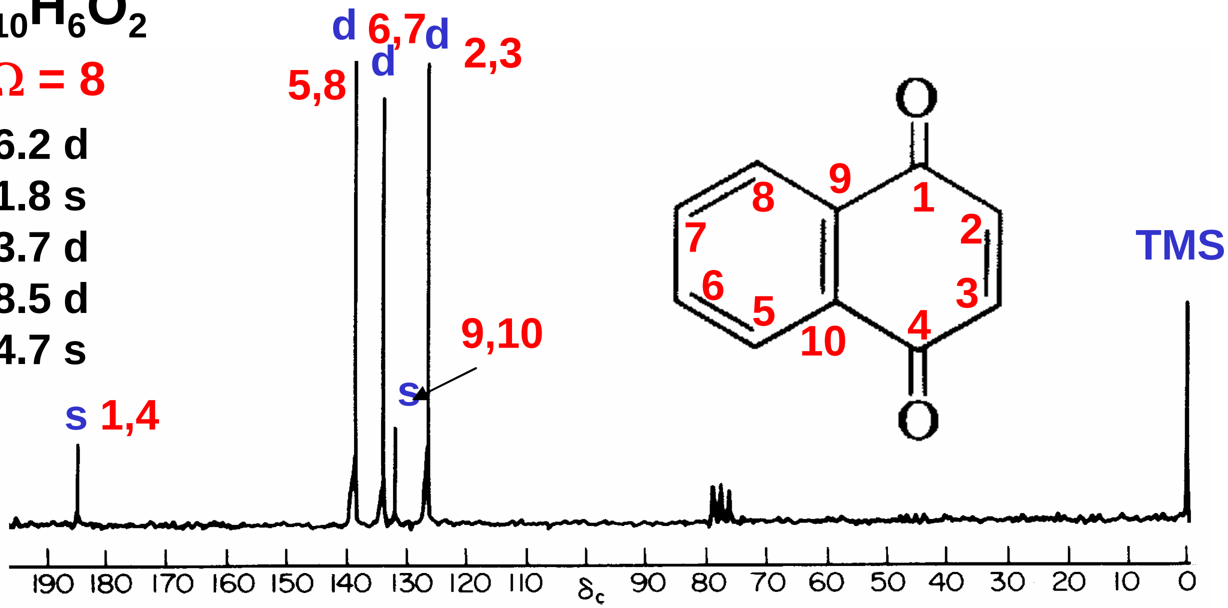


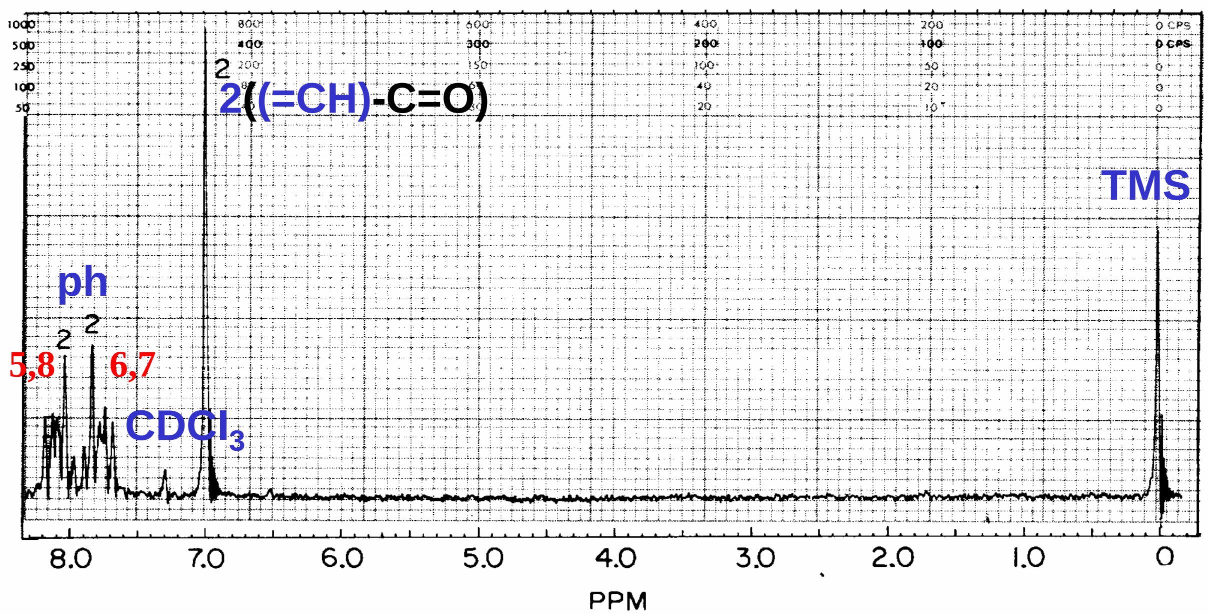


$C_{10}H_6O_2$

$\Omega = 8$

126.2 d
131.8 s
133.7 d
138.5 d
184.7 s



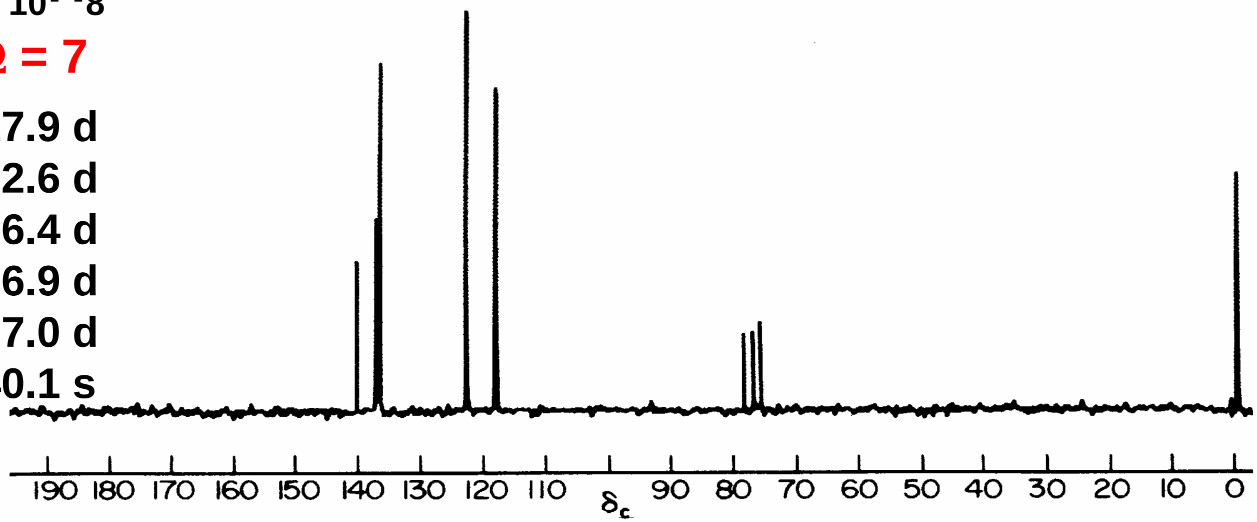


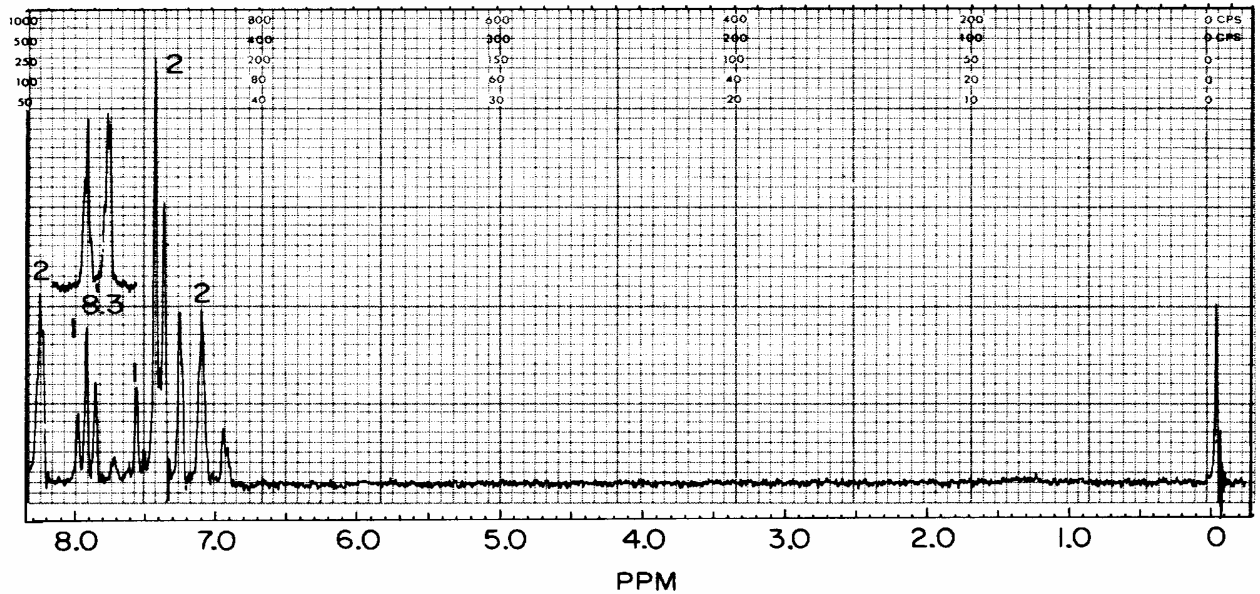
Problem 18

$C_{10}H_8$

$\Omega = 7$

117.9 d
122.6 d
136.4 d
136.9 d
137.0 d
140.1 s

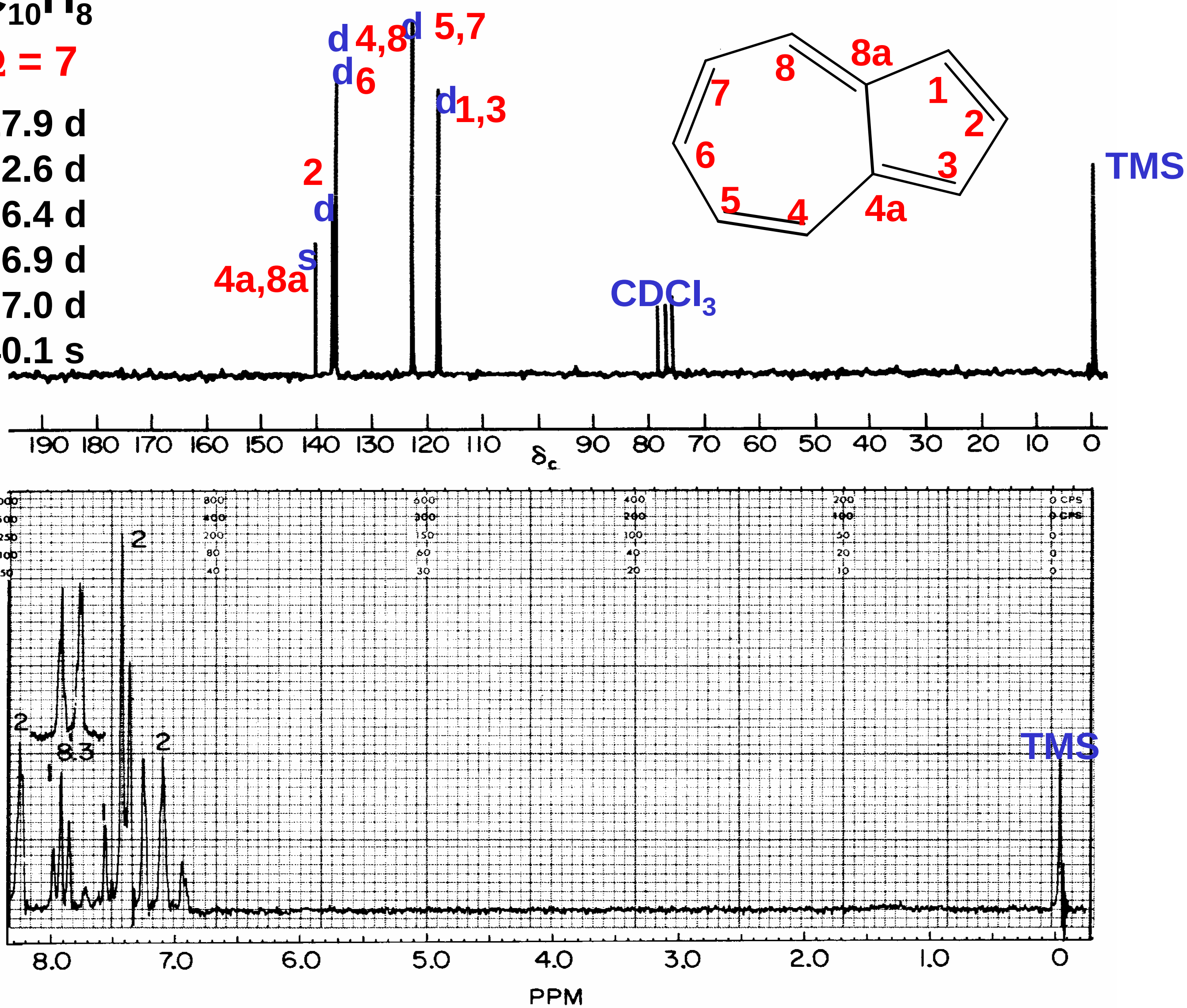




$C_{10}H_8$

$\Omega = 7$

117.9 d
122.6 d
136.4 d
136.9 d
137.0 d
140.1 s

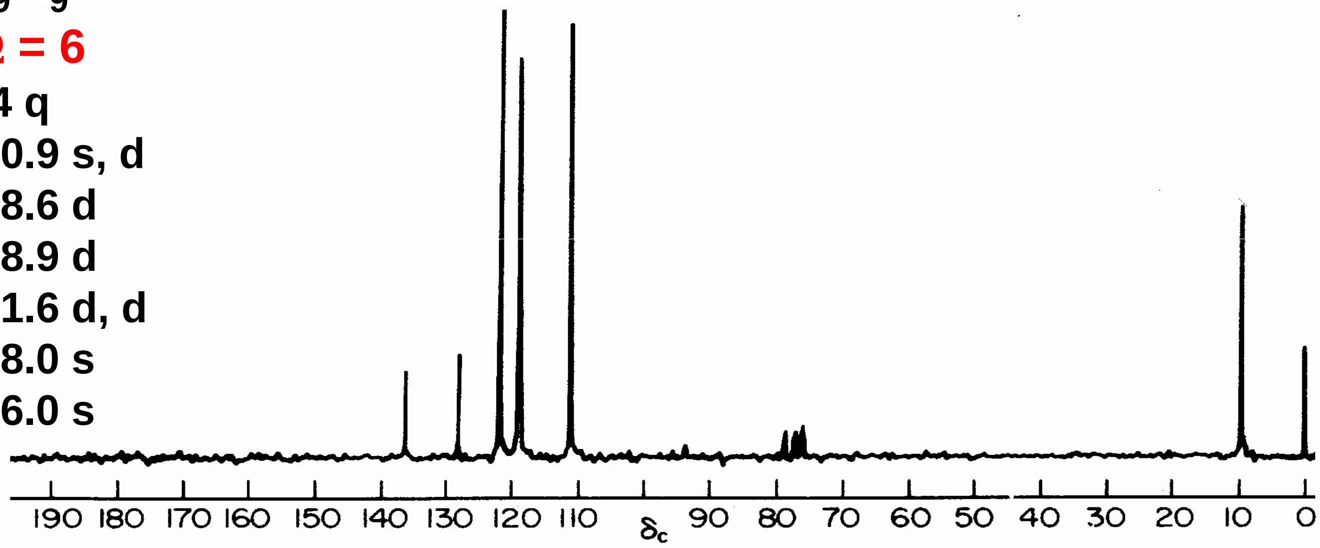


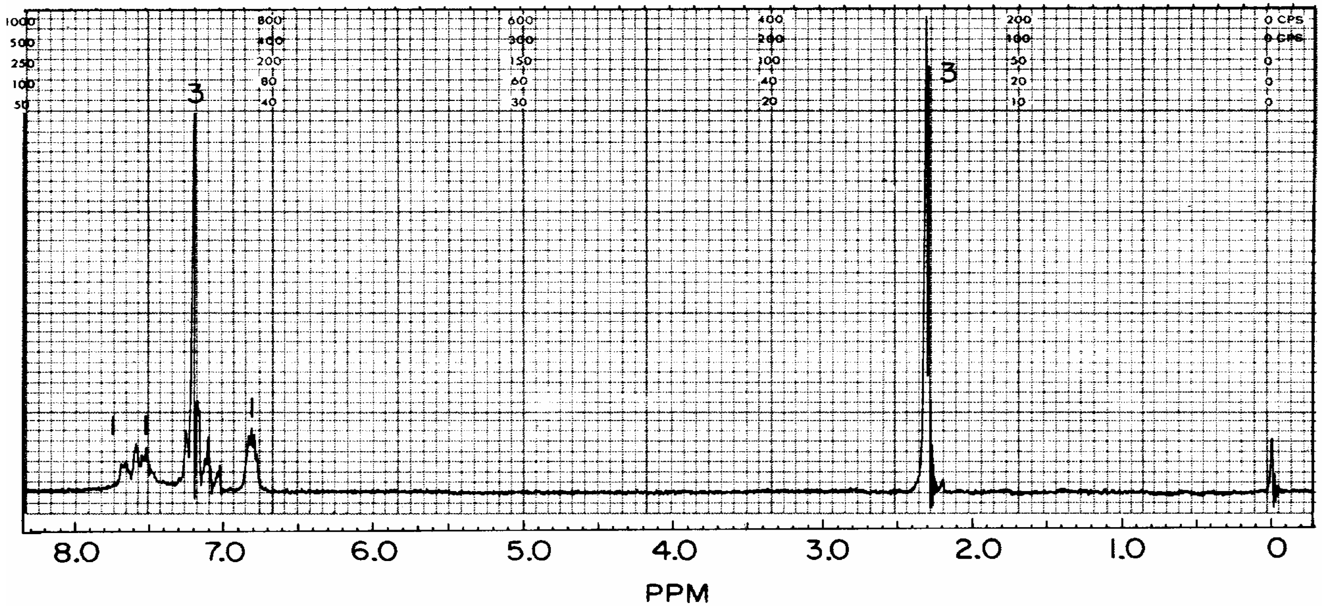
Problem 19

C_9H_9N

$\Omega = 6$

9.4 q
110.9 s, d
118.6 d
118.9 d
121.6 d, d
128.0 s
136.0 s

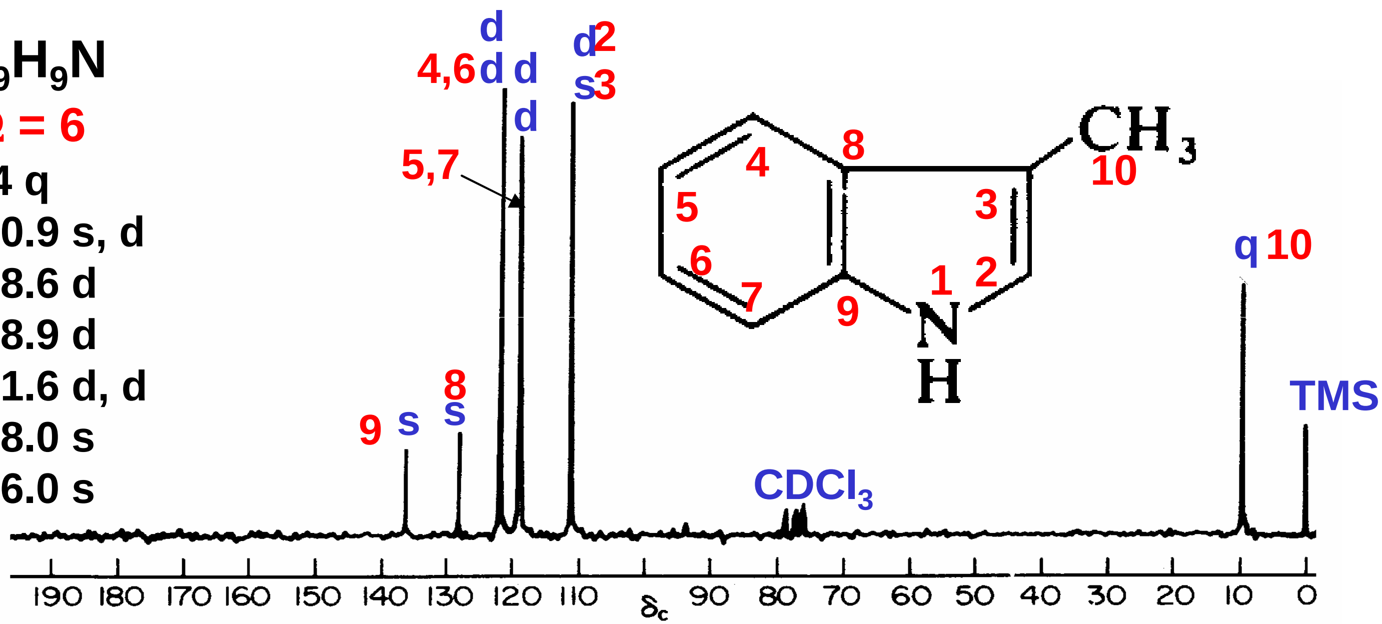


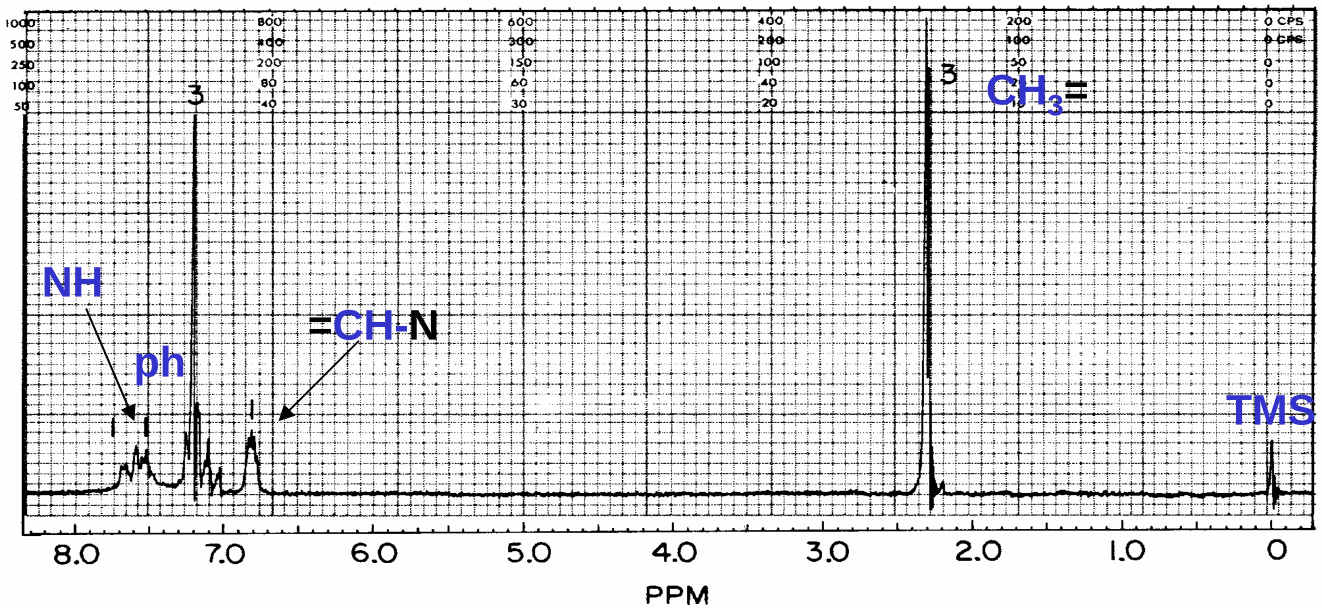


C_9H_9N

$\Omega = 6$

9.4 q
110.9 s, d
118.6 d
118.9 d
121.6 d, d
128.0 s
136.0 s



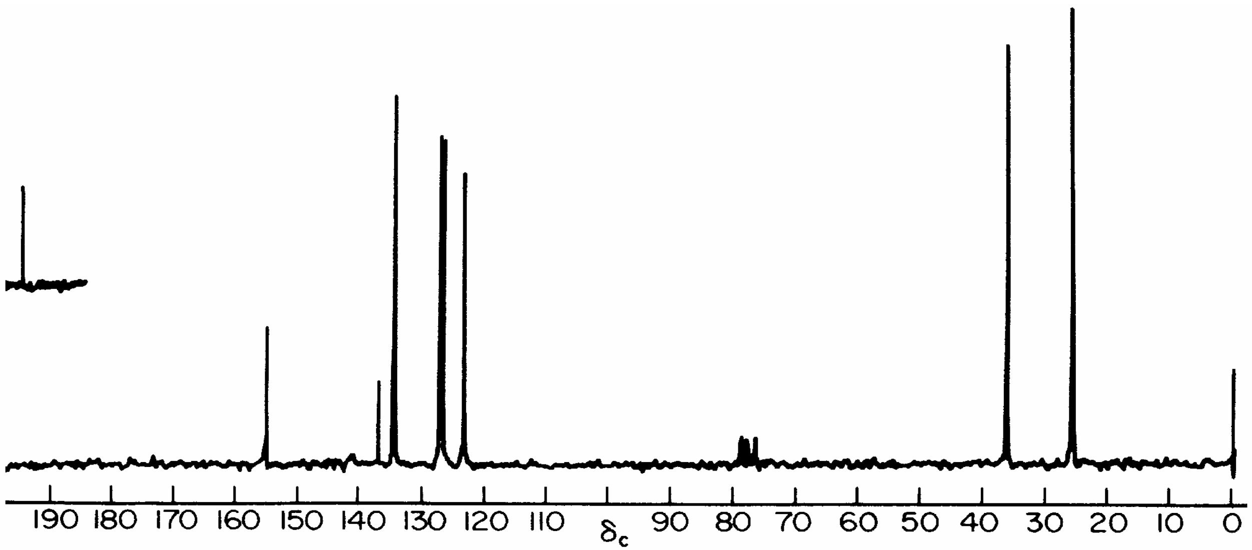


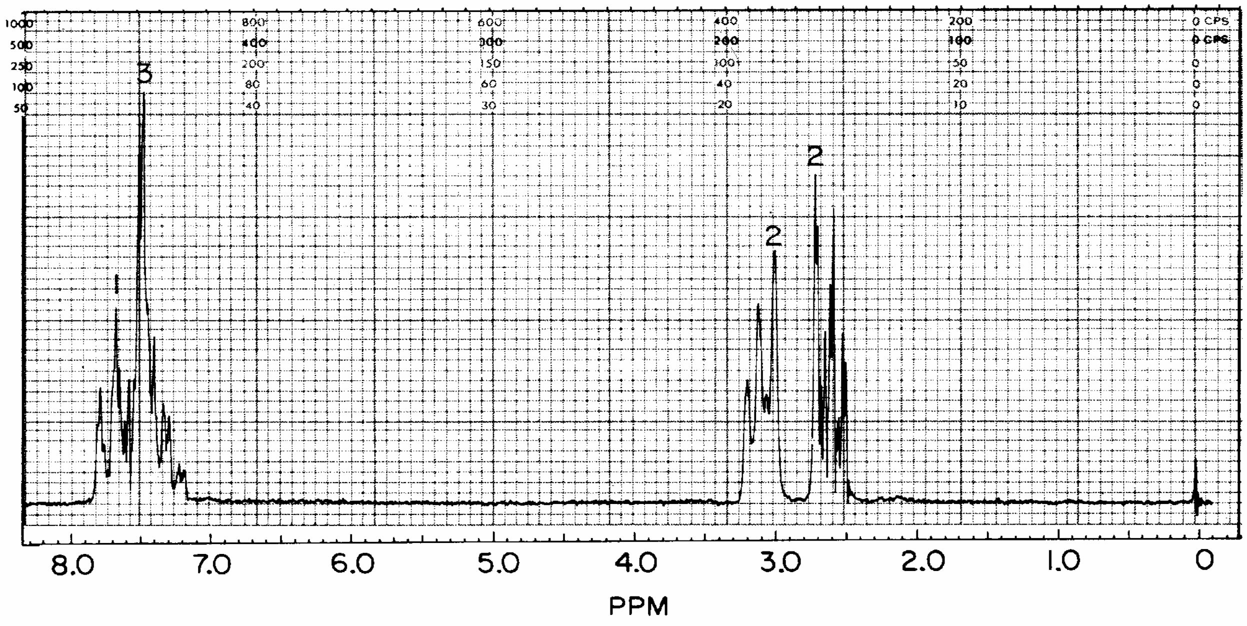
Problem 20

C_9H_8O

$\Omega = 6$

25.6 t
36.0 t
123.3 d
126.6 d
127.0 d
134.3 d
136.9 s
154.9 s
206.2 s

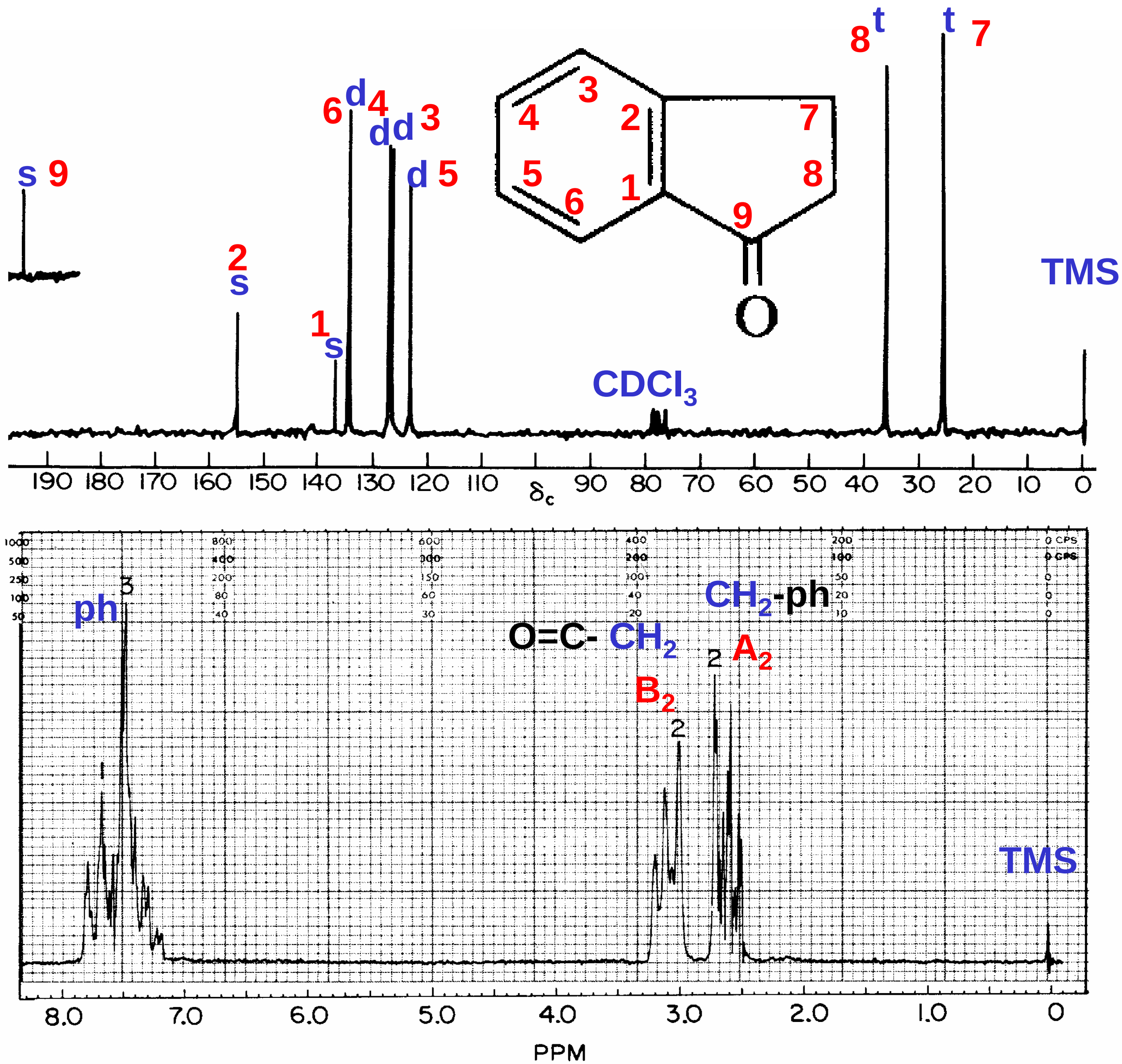




C_9H_8O

$\Omega = 6$

25.6 t
36.0 t
123.3 d
126.6 d
127.0 d
134.3 d
136.9 s
154.9 s
206.2 s

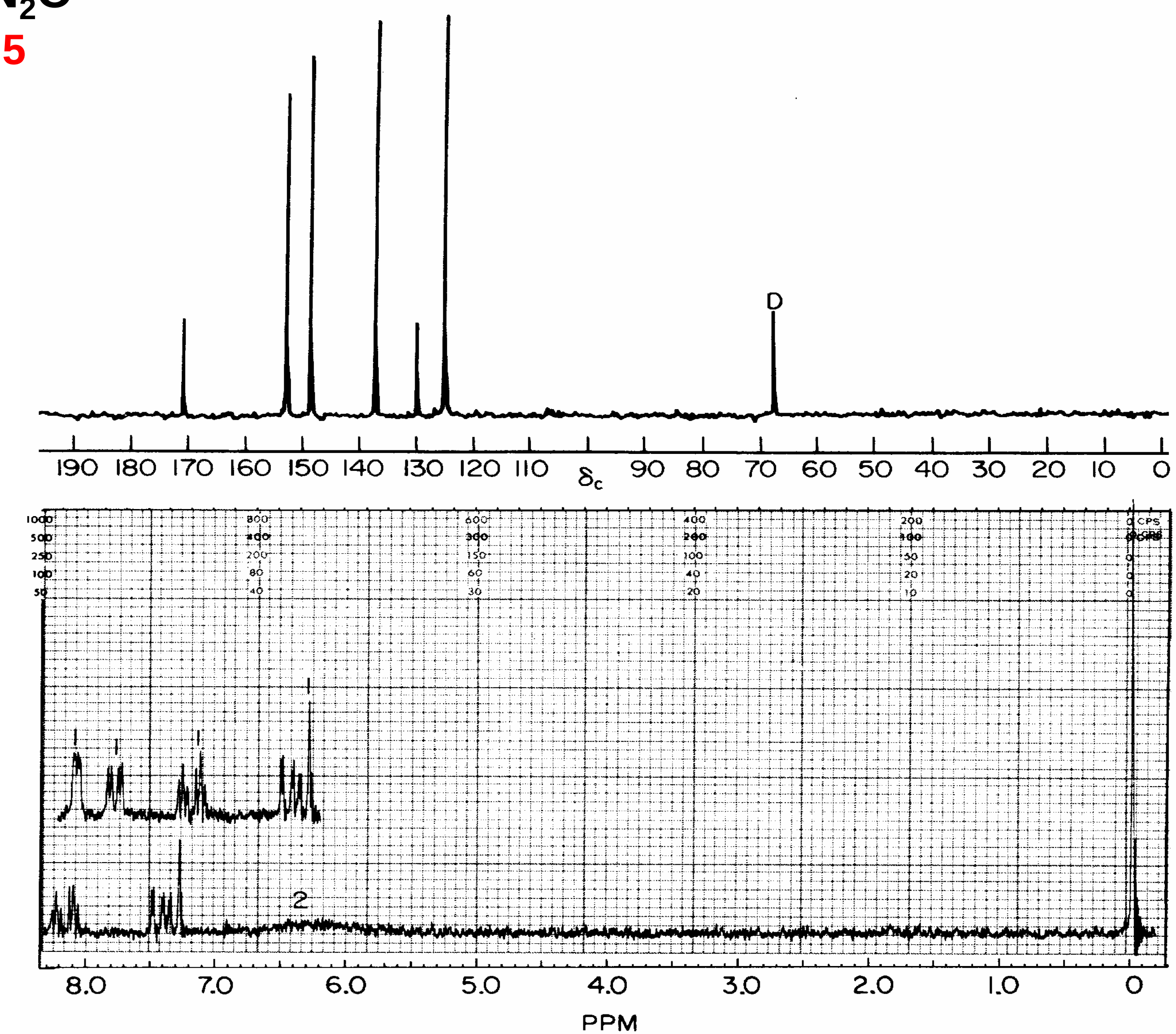


Problem 21

$C_6H_6N_2O$

$\Omega = 5$

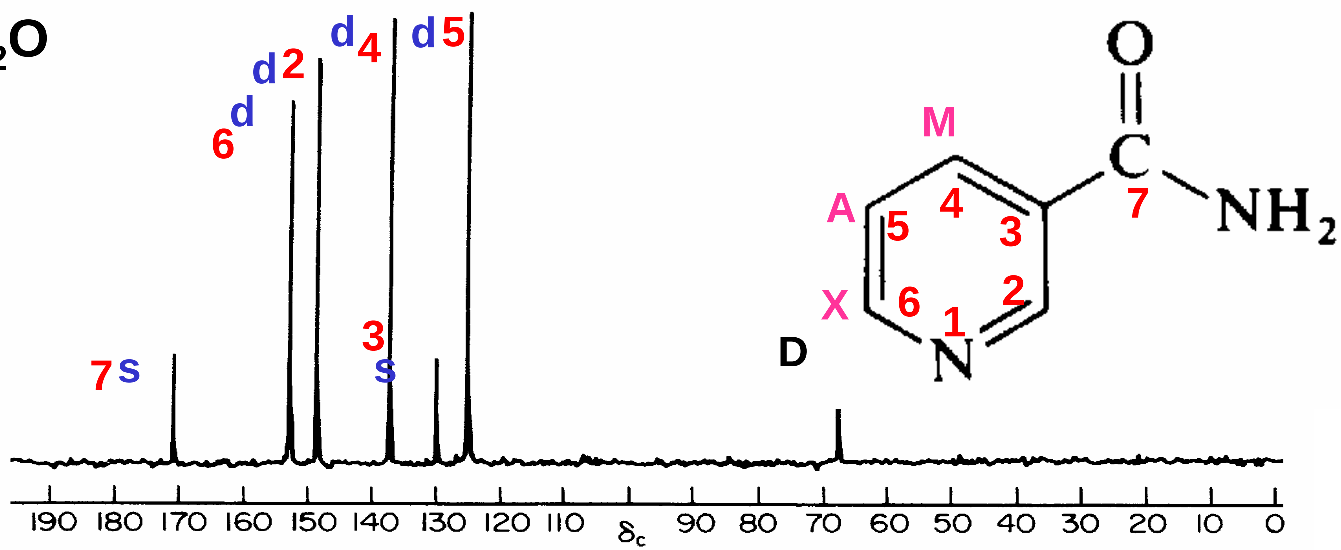
124.9 d
129.6 s
137.0 d
148.3 d
152.5 d
170.6 s

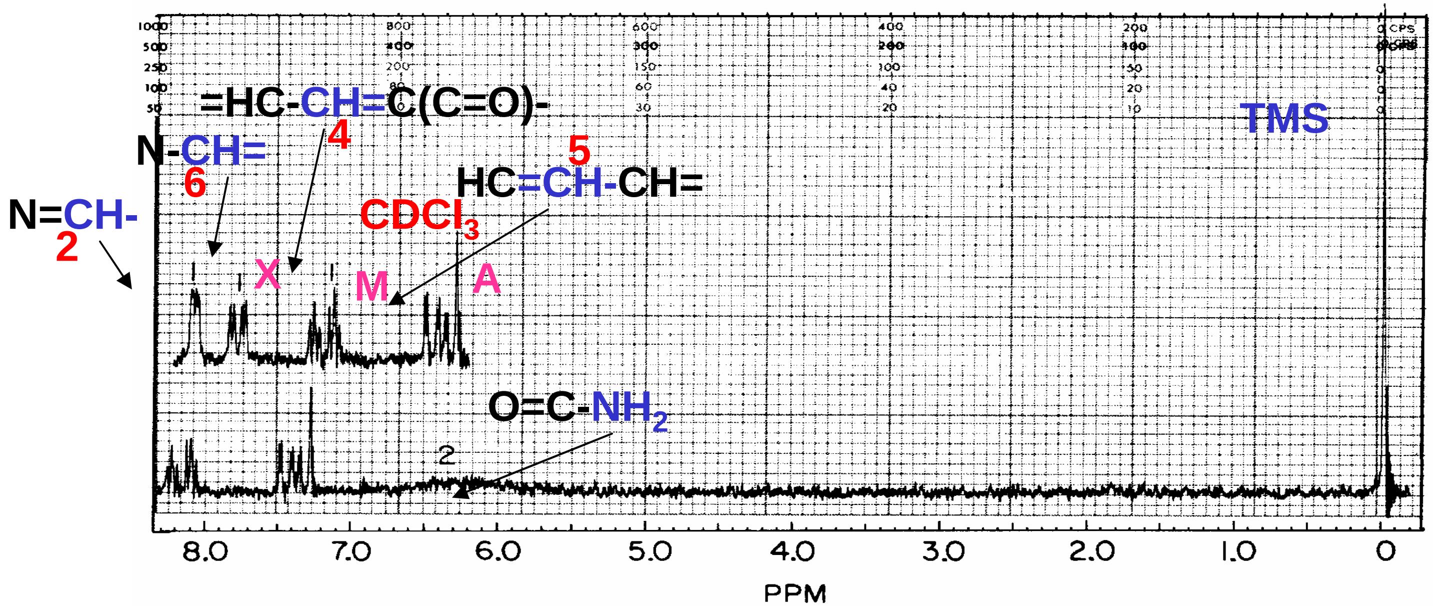


$C_6H_6N_2O$

$\Omega = 5$

124.9 d
129.6 s
137.0 d
148.3 d
152.5 d
170.6 s



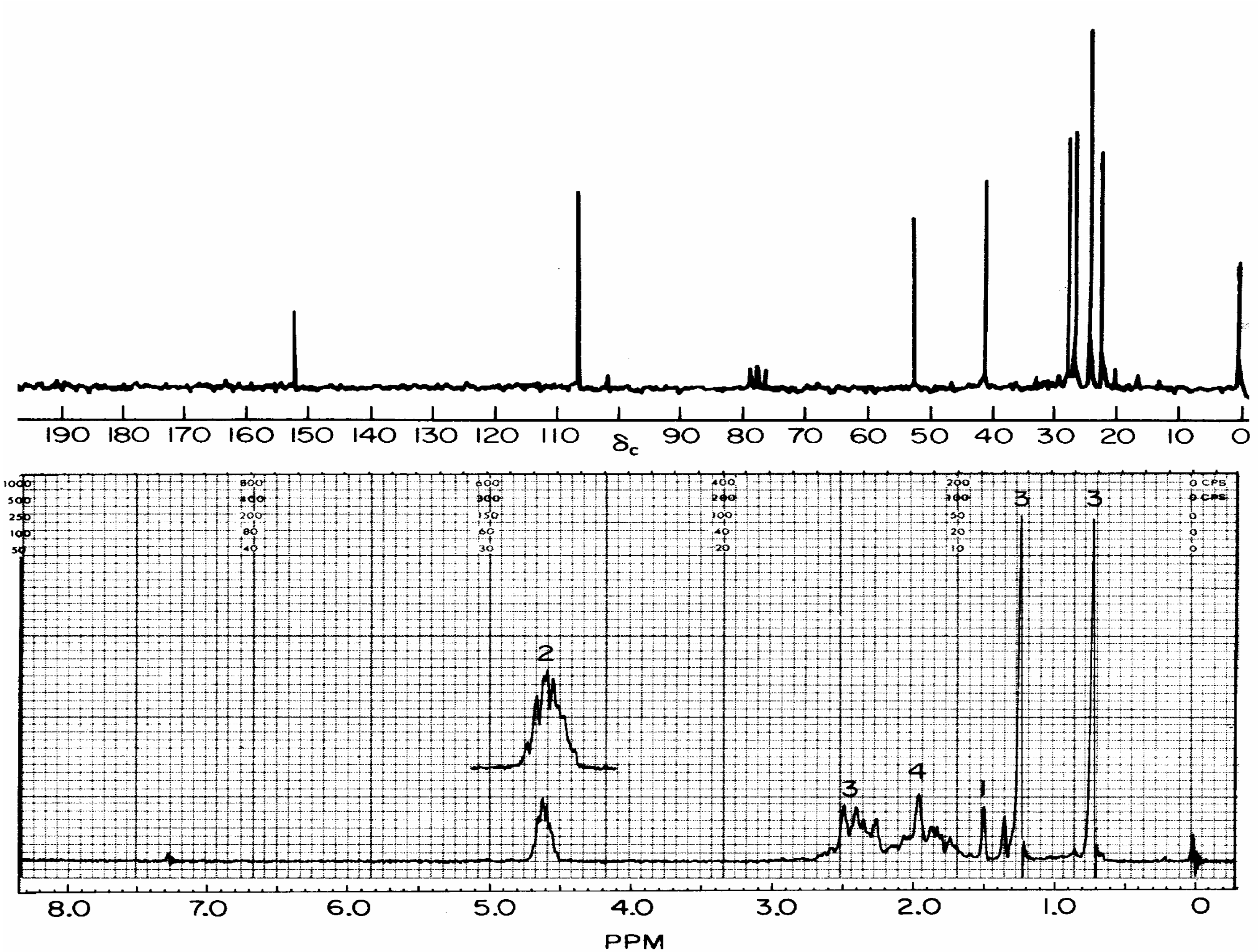


Problem 22

$C_{10}H_{16}$

$\Omega = 3$

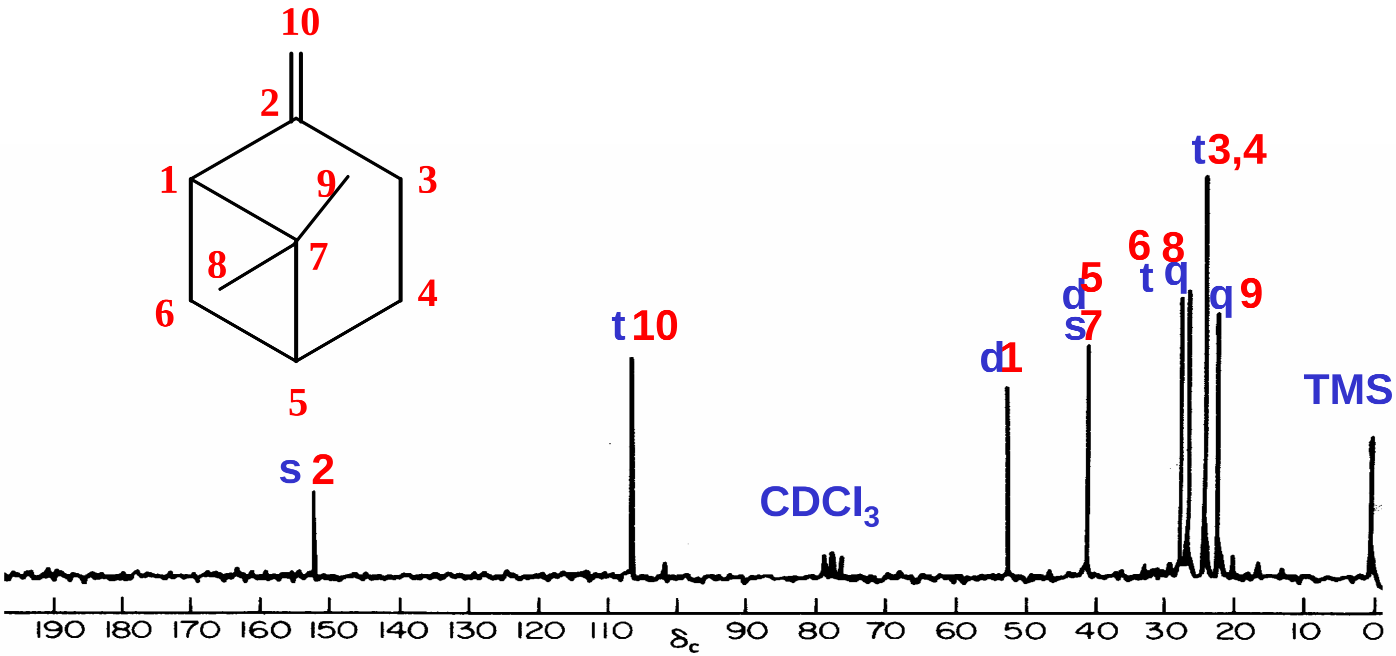
21.8 q
23.6 t
26.1 q
27.0 t
40.5 s, d
51.9 d
106.0 t
151.6 s

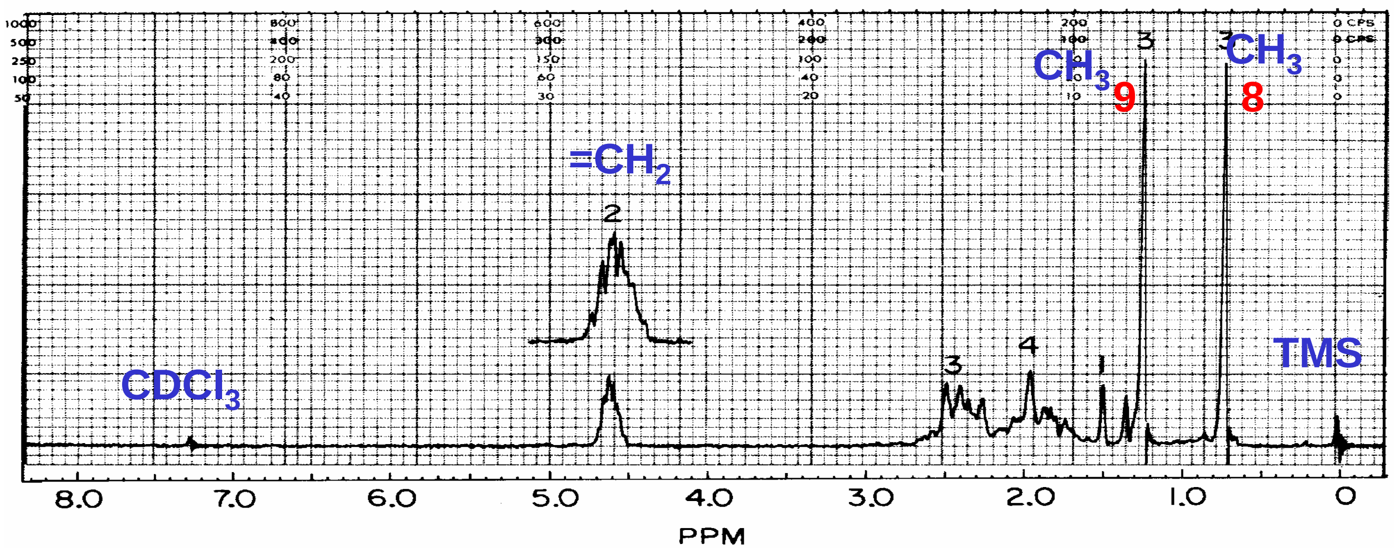


$C_{10}H_{16}$

$\Omega = 3$

21.8 q
23.6 t
26.1 q
27.0 t
40.5 s, d
51.9 d
106.0 t
151.6 s

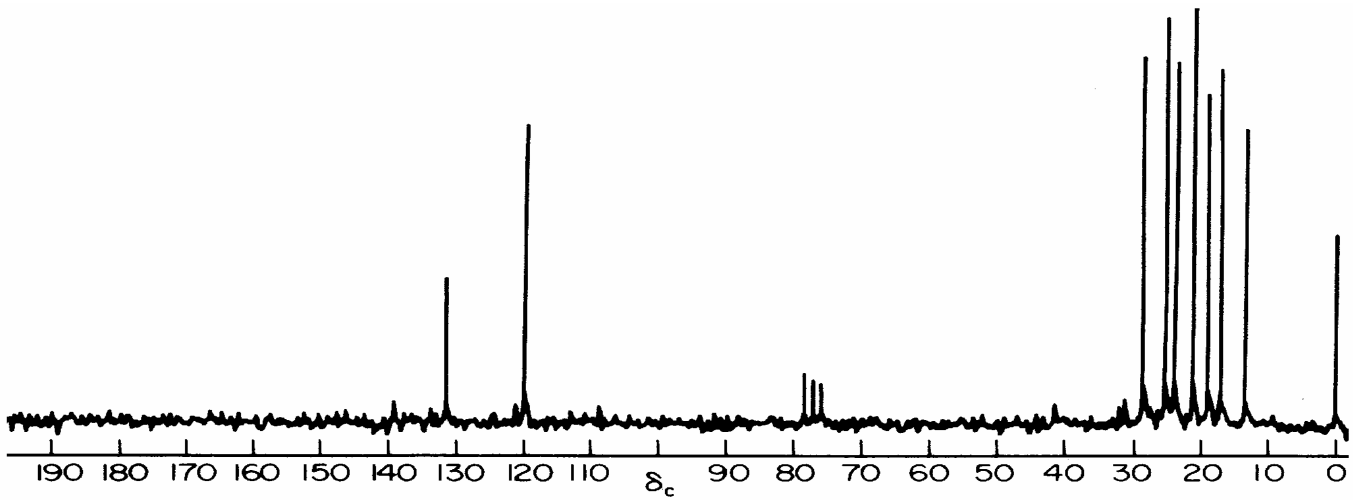


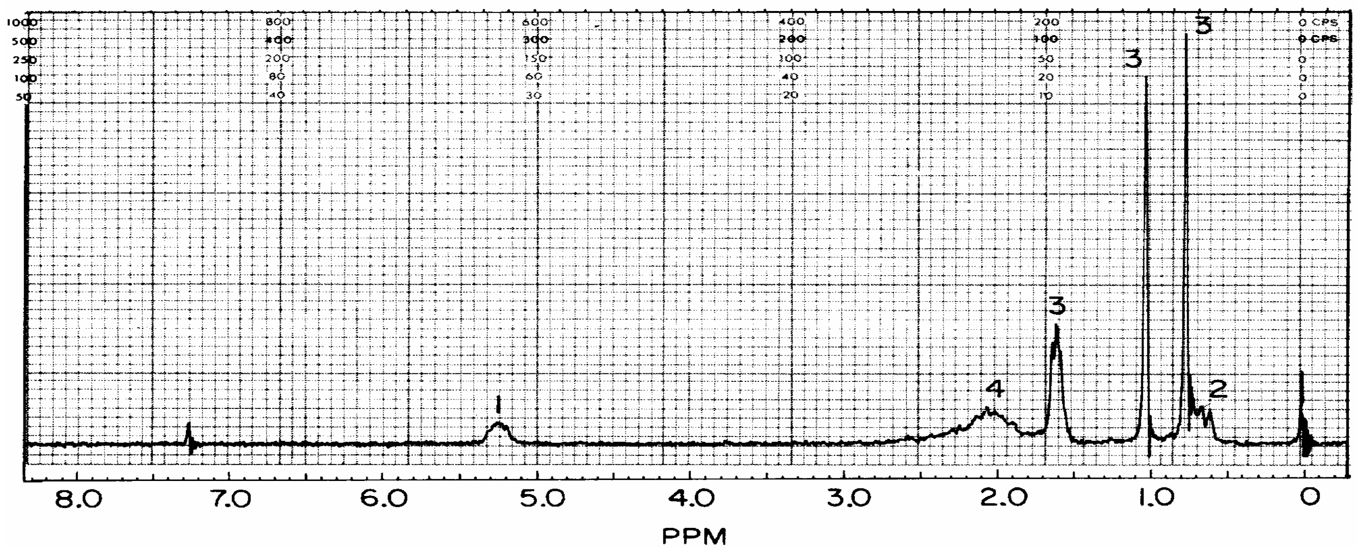


Problem 23

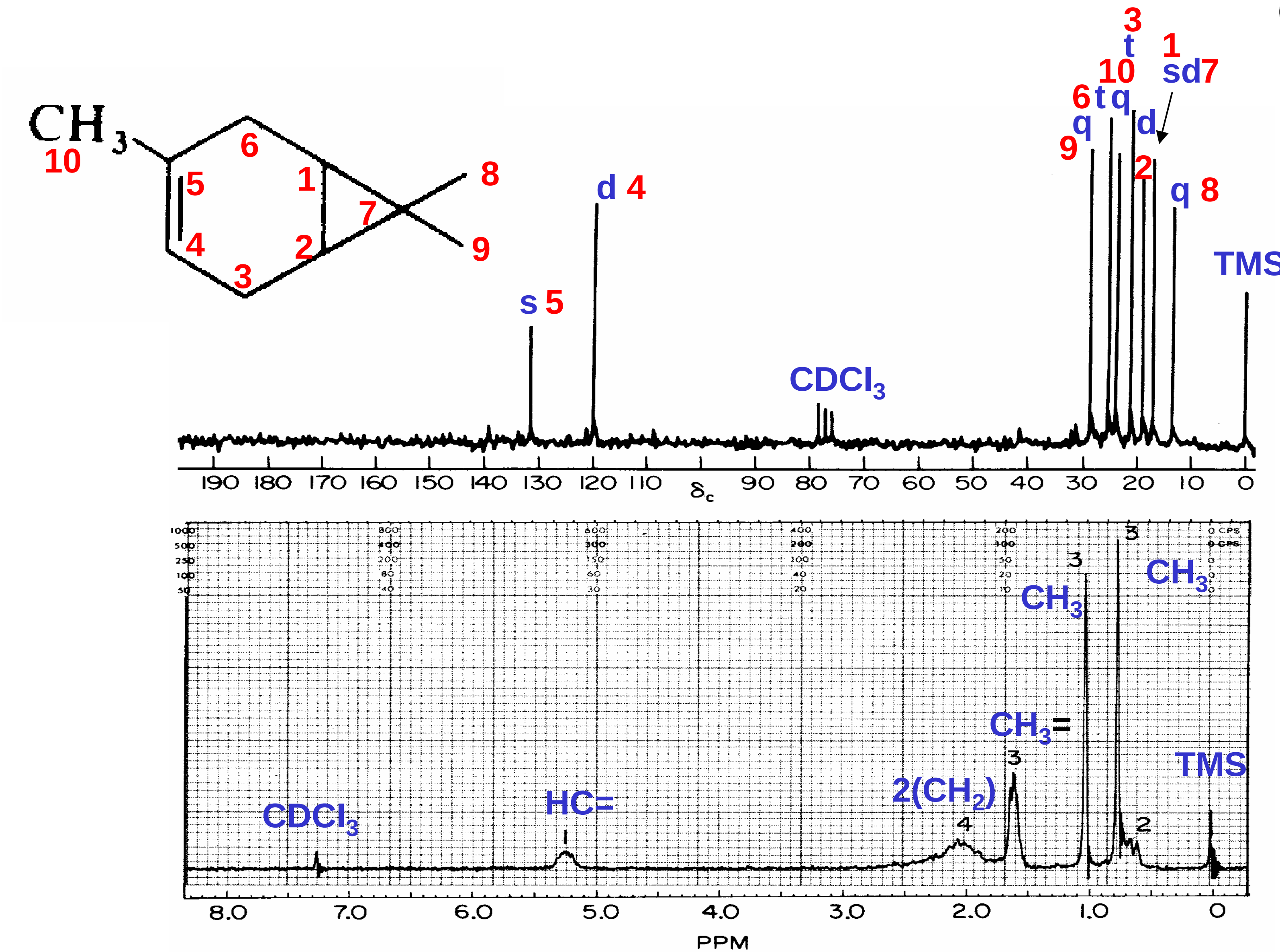
$C_{10}H_{16}$

$\Omega = 3$





113.1 q
16.7 s
16.8 d
18.7 d
20.8 t
23.6 q
24.9 t
28.4 q
119.5 d
131.2 s

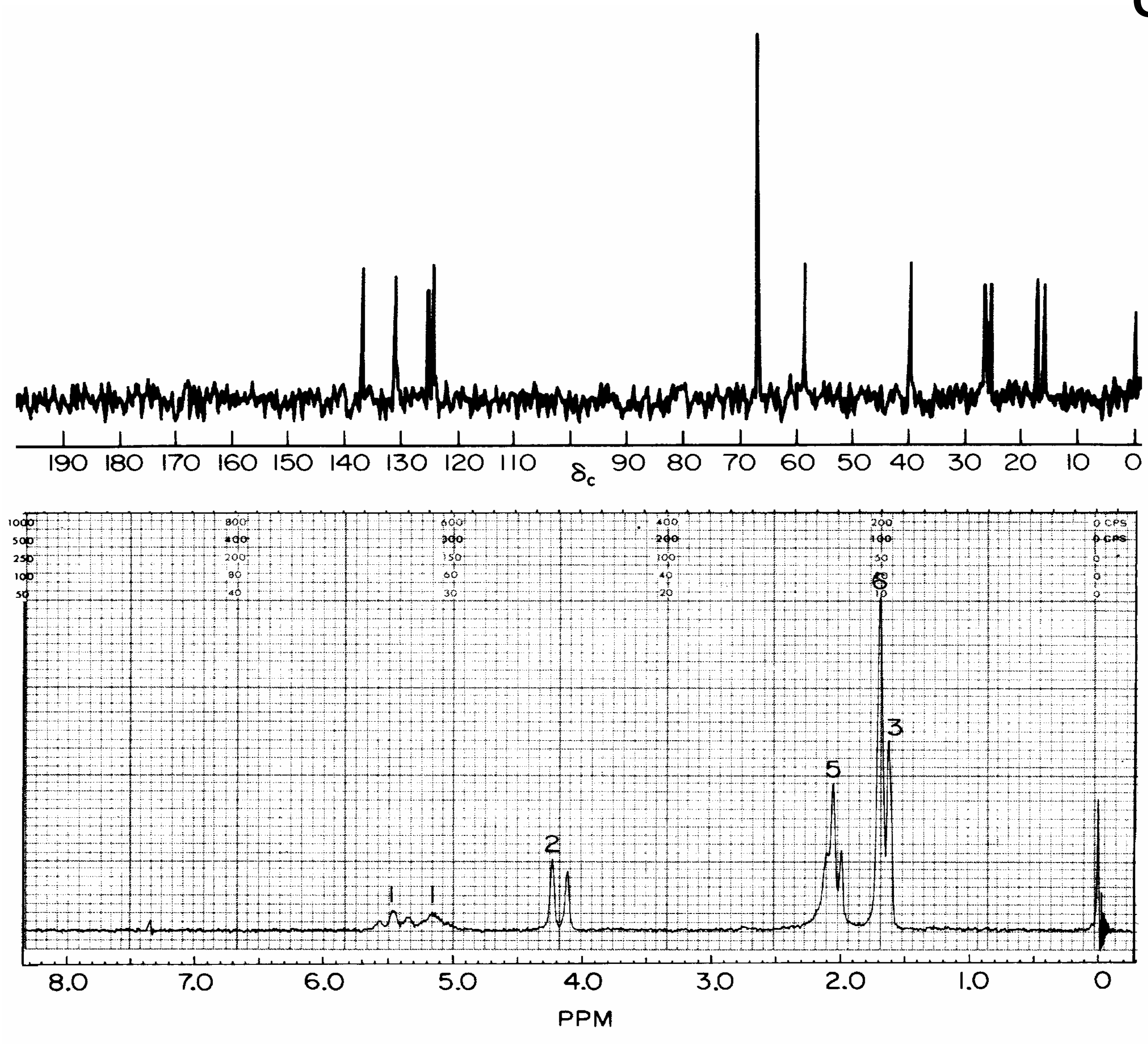


$C_{10}H_{16}$

$\Omega = 3$

113.1 q
16.7 s
16.8 d
18.7 d
20.8 t
23.6 q
24.9 t
28.4 q
119.5 d
131.2 s

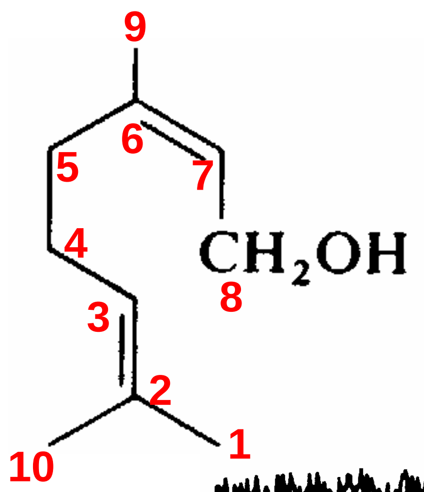
Problem 24



$C_{10}H_{18}O$

$\Omega = 2$

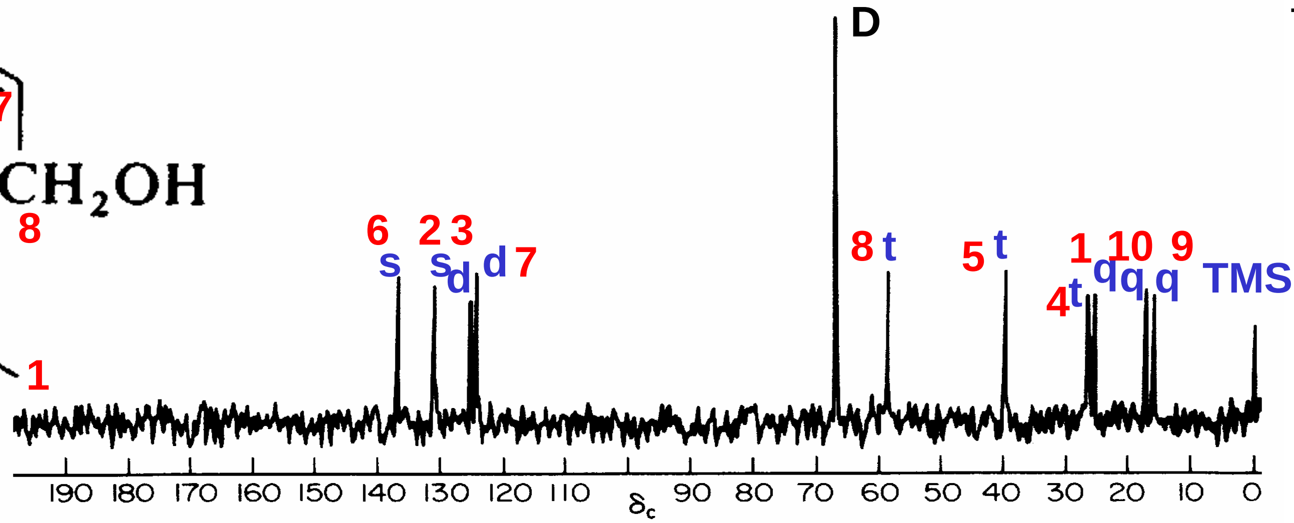
16.1 q
17.6 q
25.6 q
26.8 t
39.8 t
58.6 t
124.4 d
125.3 d
131.1 s
136.9 s

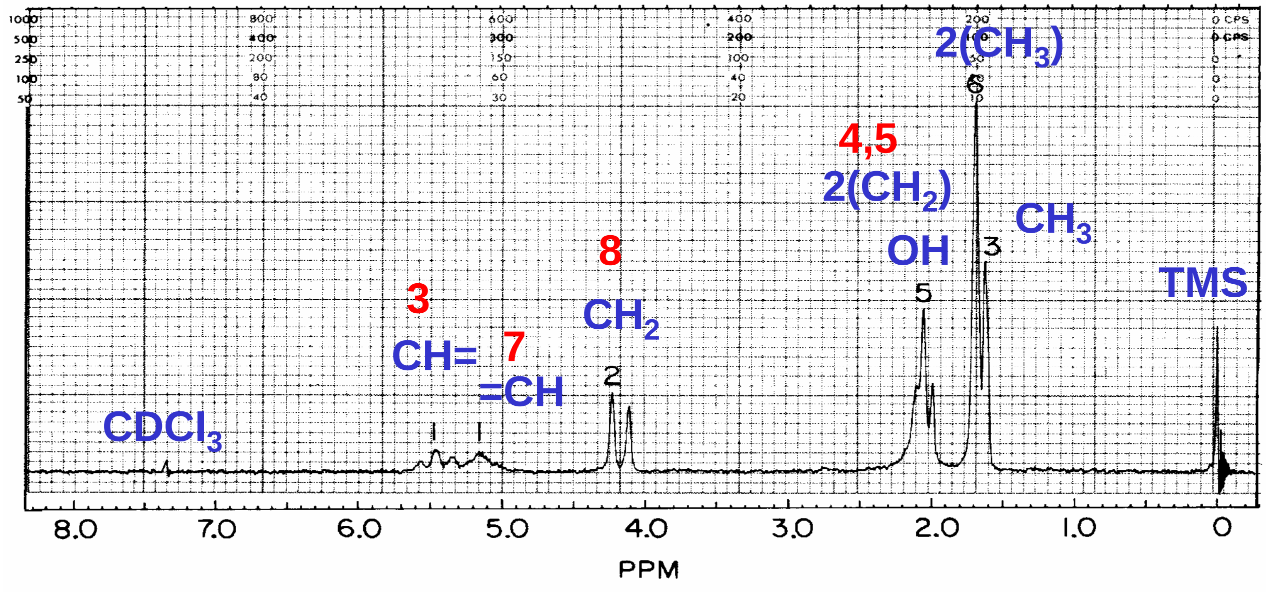


$C_{10}H_{18}O$

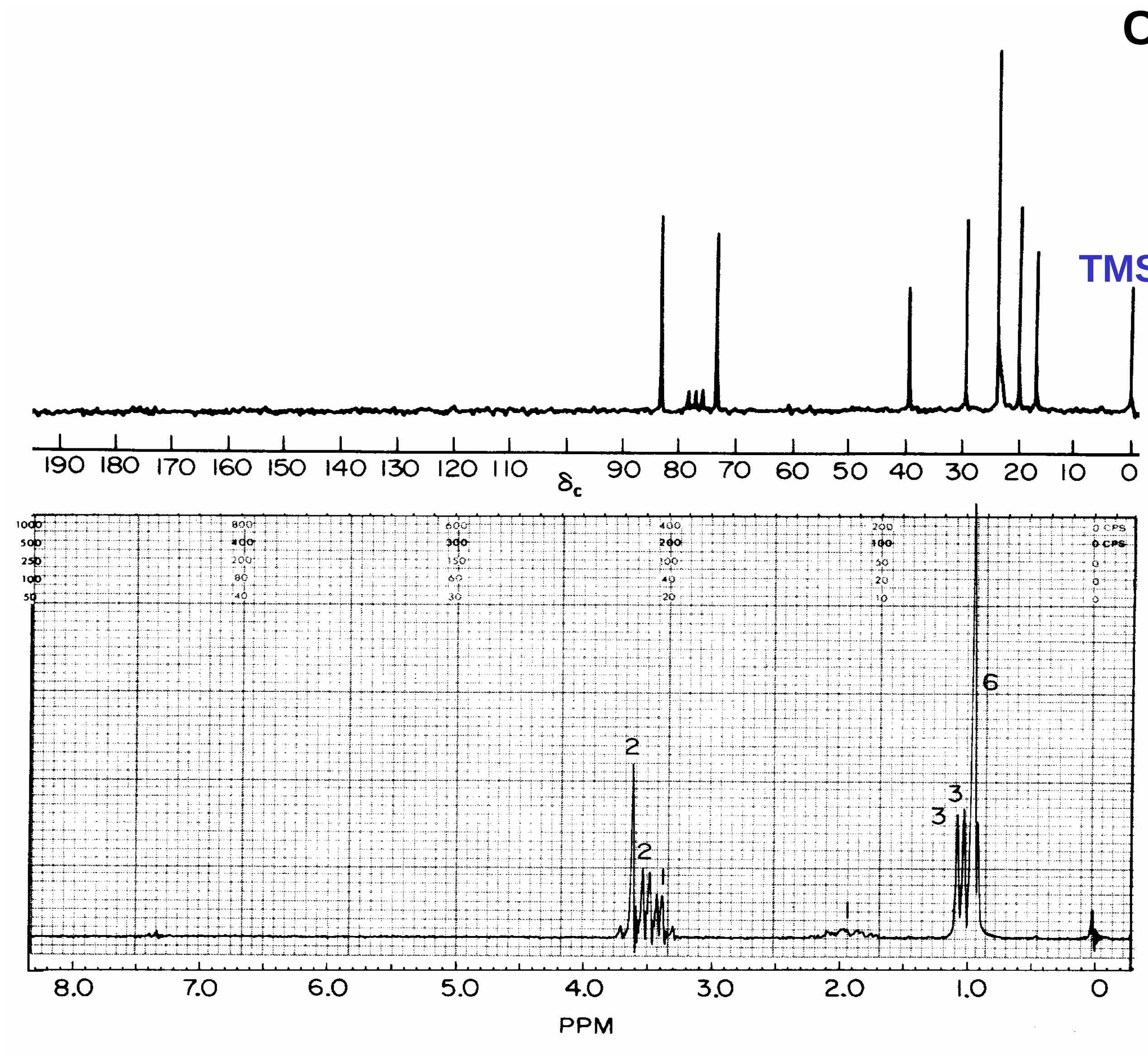
$\Omega = 2$

16.1 q
17.6 q
25.6 q
26.8 t
39.8 t
58.6 t
124.4 d
125.3 d
131.1 s
136.9 s





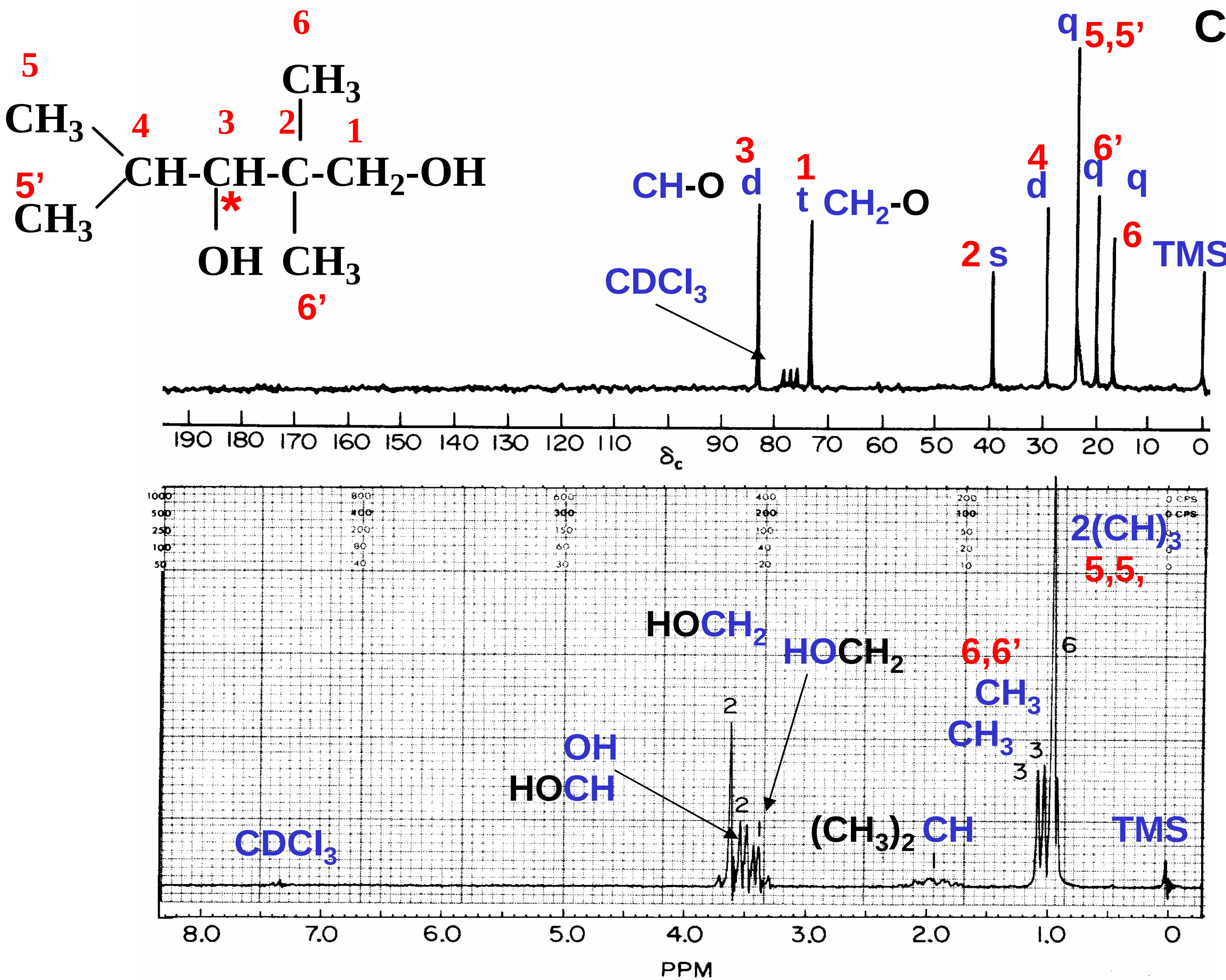
Problem 25



$C_8H_{18}O_2$

$\Omega = 0$

16.7 q
19.7 q
23.3 q,q
29.2 d
39.1 s
73.1 t
83.0 d

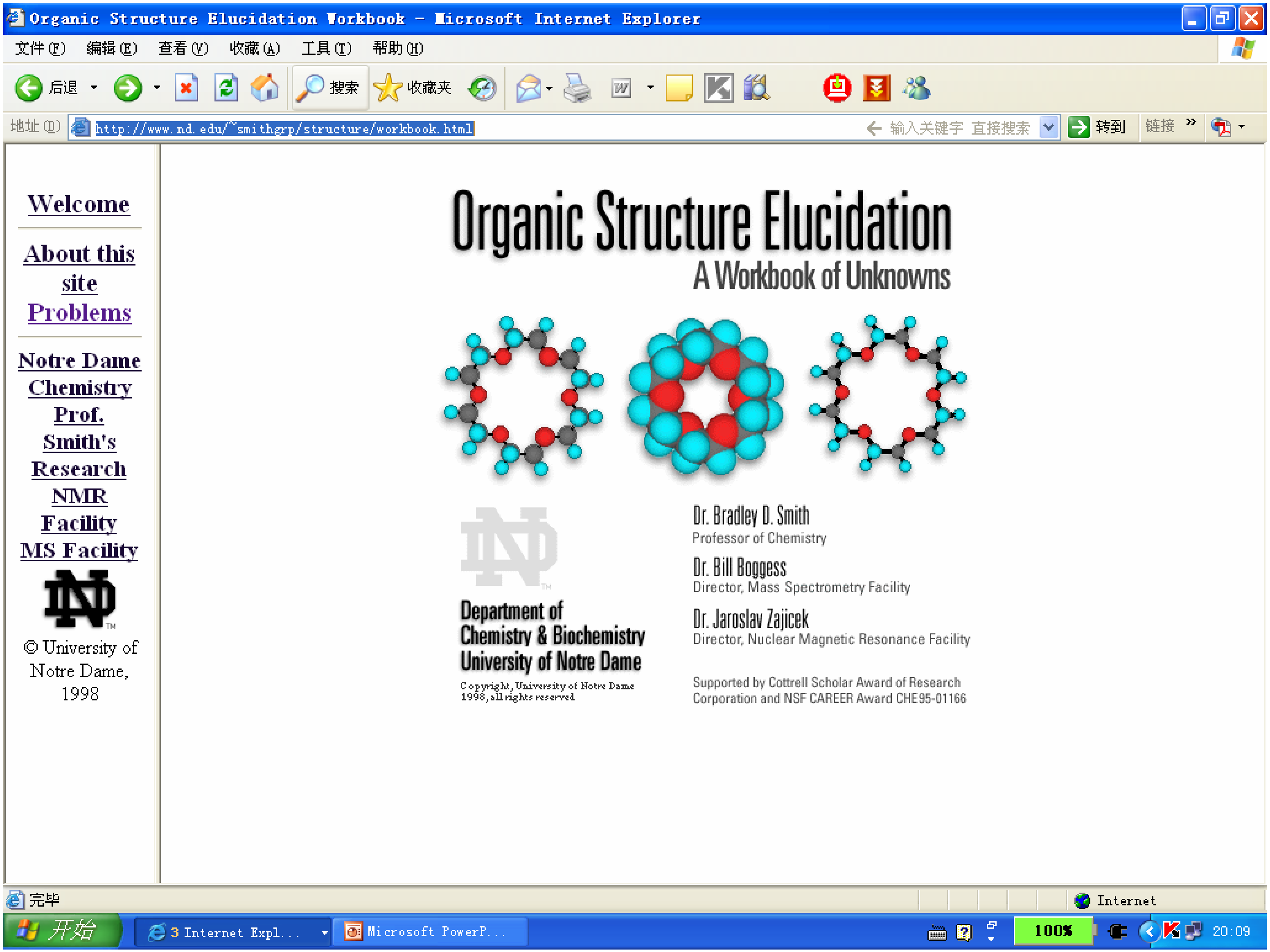


$C_8H_{18}O_2$

$\Omega = 0$

16.7 q
19.7 q
23.3 q,q
29.2 d
39.1 s
73.1 t
83.0 d

http://www.nd.edu/~smithgrp/structure/workbook.html

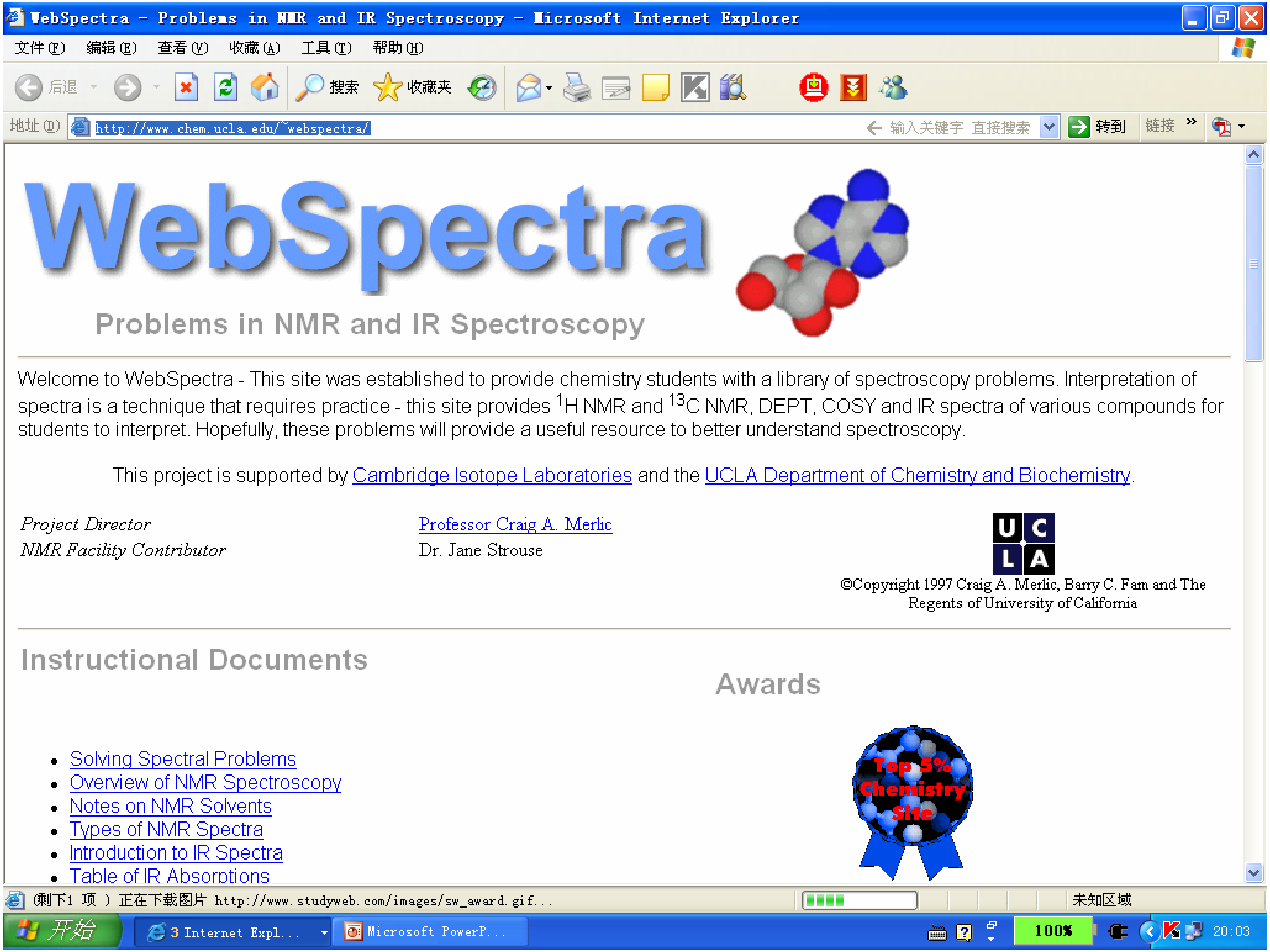


http://chemistry2.csudh.edu/newstuff/nmrspectra.html

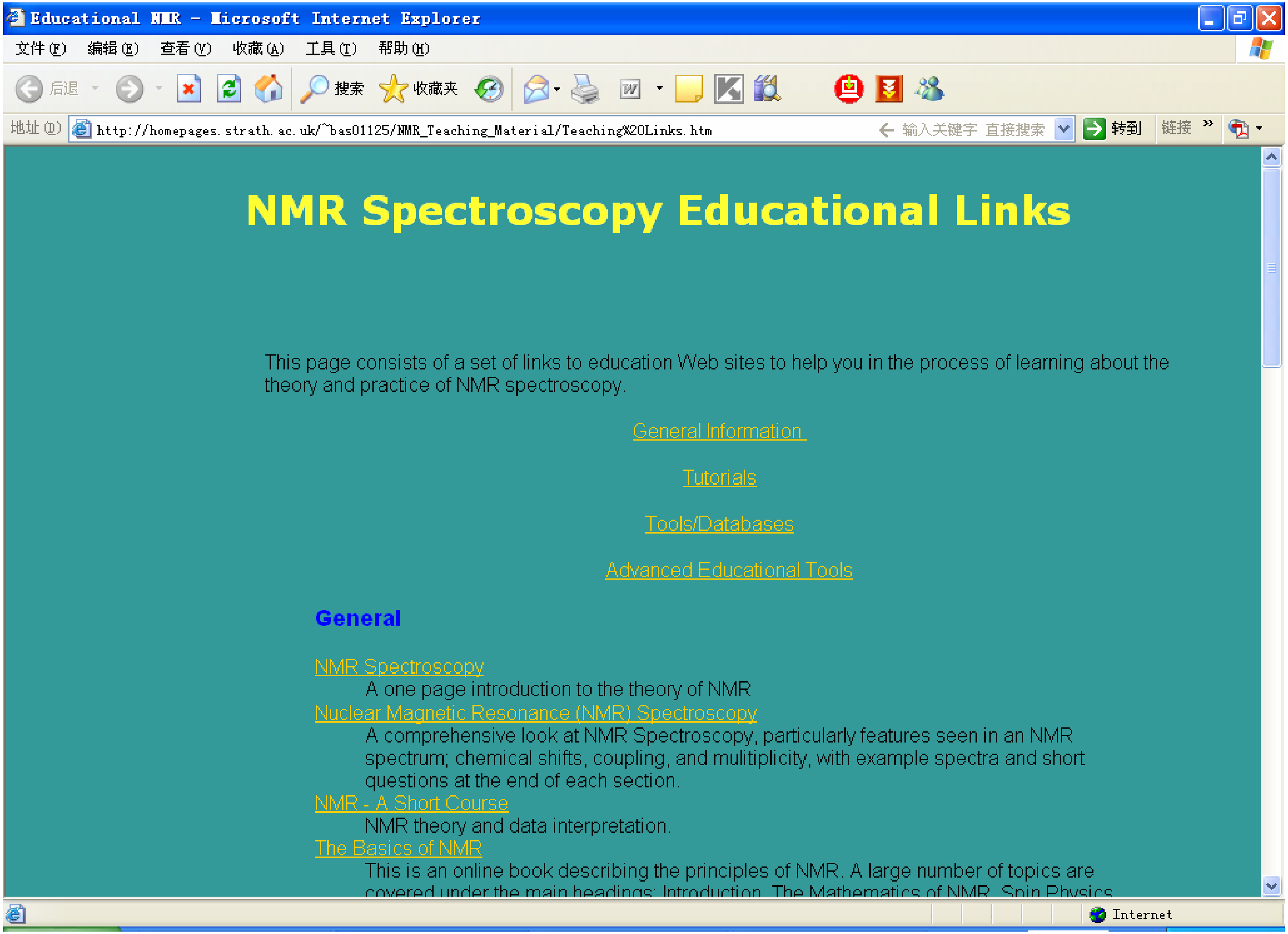
- **Assign Peaks**: A spectrum and a structure will be displayed. To assign the spectrum, you must first click on a proton (or group of protons) in the structural formula. When you click on a proton, a • will appear slightly below and to the right of the proton chosen. If the structure contains equivalent protons, only one will be clickable. You will know that you are on a clickable proton when the converts to . Once you have selected a proton, click on the proper resonance in the spectrum. If the proper assignmment is made, the • will be converted into a • and the word "correct" will appear in the cell in the top frame. Otherwise the • will remain and the word "incorrect" will appear.
- **Identify Compound**: A spectrum will be displayed and below the spectrum will be a list of five compounds. Click on the bubble in front of the compound corresponding to the displayed spectrum. Results appear in top frame.
- **Assignment Tutor**: The spectrum and structure are displayed as in the "Assign Peaks" option, but clicking on a resonance causes a • to appear below the appropriate proton(s).

Note to Netscape users: Of late I have been encountering problems loading complex framed pages into Navigator, if I'm also running Internet Explorer. The problem goes away if I reboot the computer and run Navigator directly without having run IE. The pages always seem to load with IE and there are no errors in the page syntax to cause loading problems. Whether this is a result of some IE/Navigator conflict, I don't know, but it does cause one to ponder.
The current database contains over 150 compounds. When I am satisfied with the performance of the page, I'll bundle it all as a zip file for others to download. To help with this, I would greatly appreciate feedback and have a link below for that purpose. Thanks.
George Wiger
5/10/99
load the page
Feedback to George

http://www.chem.ucla.edu/~webspectra/



http://homepages.strath.ac.uk/~bas01125/NMR_Teaching_Material/Teaching%20Links.htm



Educational NMR - Microsoft Internet Explorer

文件(F) 编辑(E) 查看(V) 收藏(A) 工具(T) 帮助(H)

后退 搜索 收藏夹

地址(D) http://homepages.strath.ac.uk/~bas01125/NMR_Teaching_Material/Teaching%20Links.htm 输入关键字 直接搜索 转到 链接

NMR Spectroscopy Educational Links

This page consists of a set of links to education Web sites to help you in the process of learning about the theory and practice of NMR spectroscopy.

General Information

Tutorials

Tools/Databases

Advanced Educational Tools

General

NMR Spectroscopy
A one page introduction to the theory of NMR

Nuclear Magnetic Resonance (NMR) Spectroscopy
A comprehensive look at NMR Spectroscopy, particularly features seen in an NMR spectrum; chemical shifts, coupling, and mulitiplicity, with example spectra and short questions at the end of each section.

NMR - A Short Course
NMR theory and data interpretation.

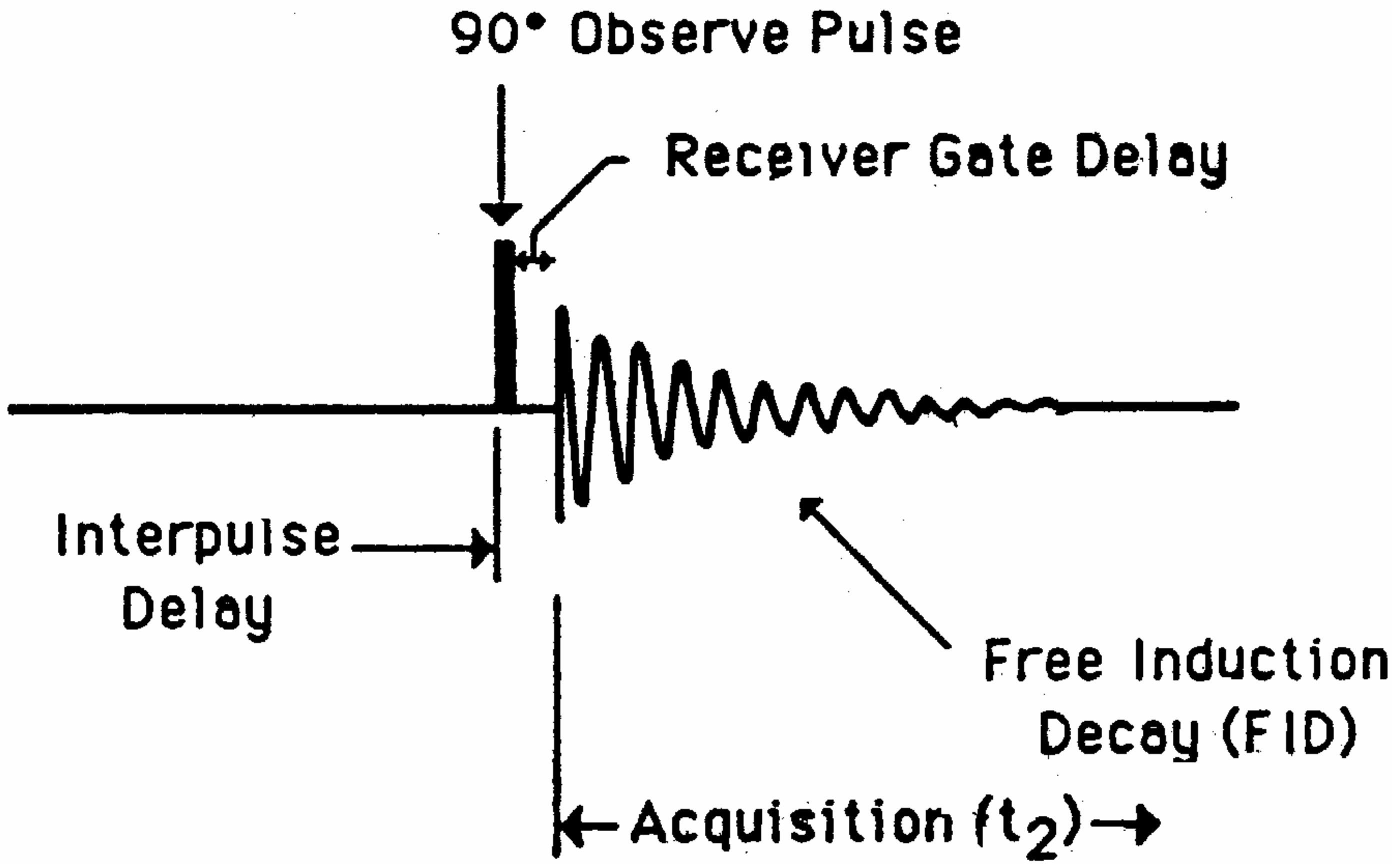
The Basics of NMR
This is an online book describing the principles of NMR. A large number of topics are covered under the main headings: Introduction, The Mathematics of NMR, Spin Physics

Internet

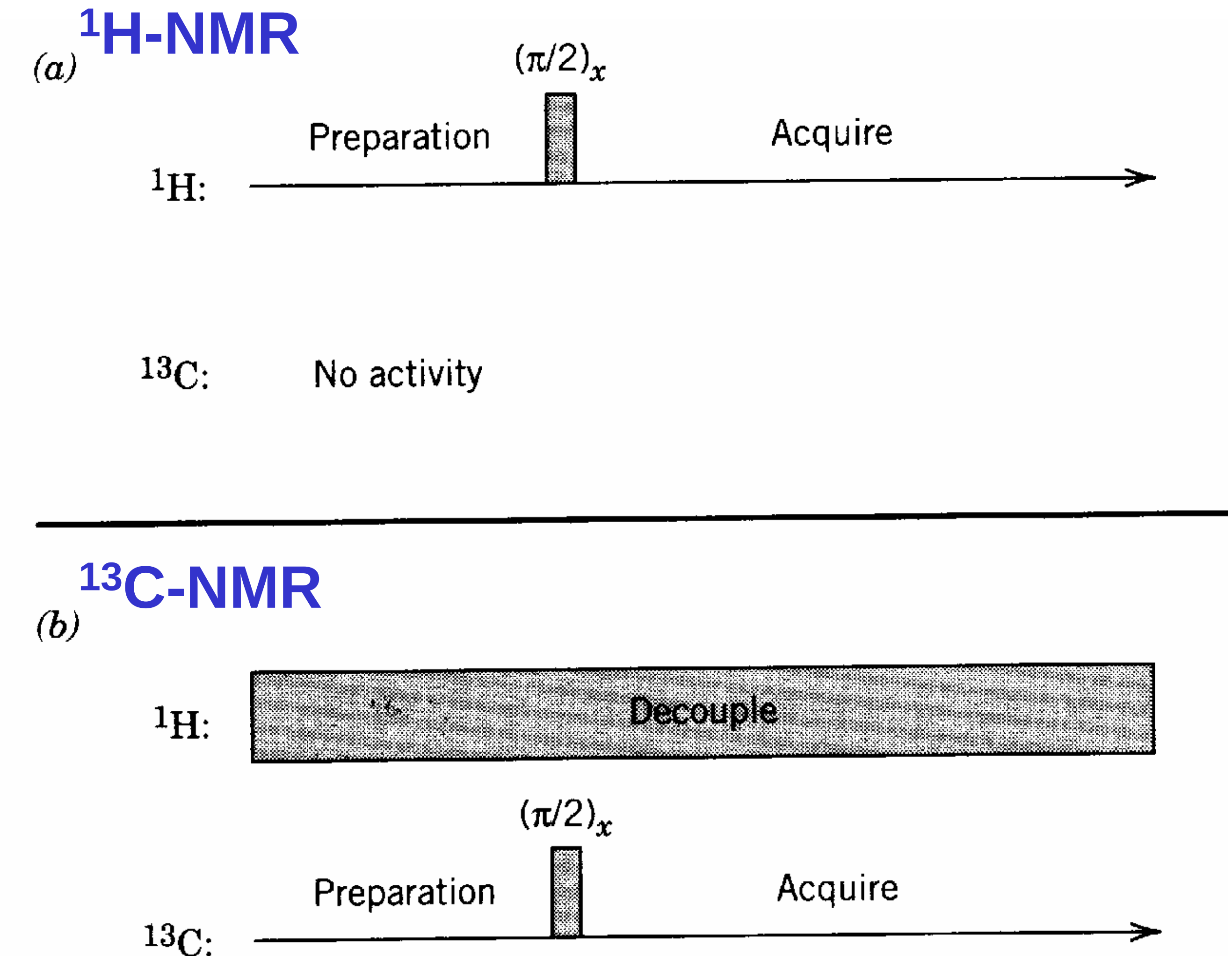
Chapter 6:

Multiple-Pulse NMR Experiments

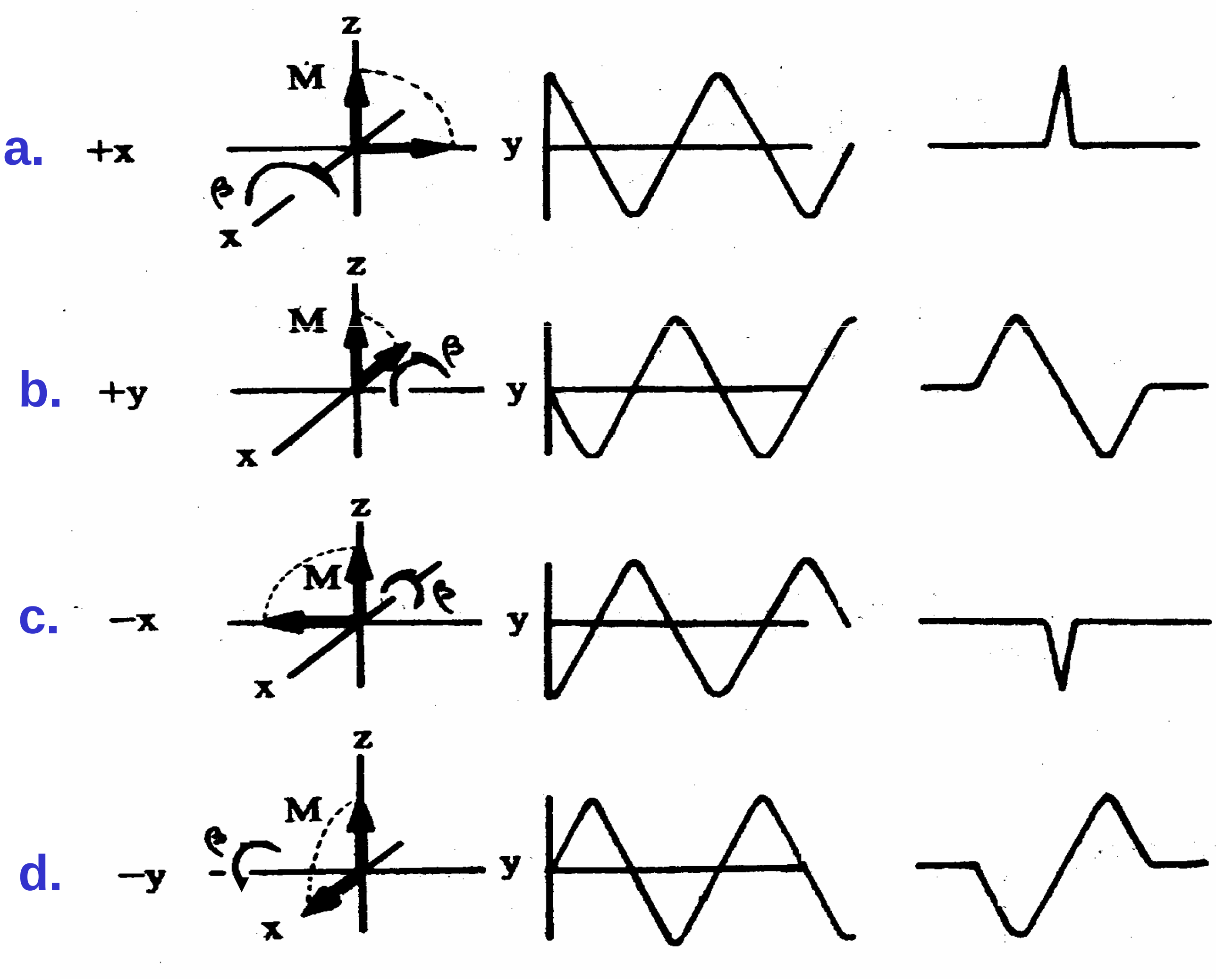
Single-Pulse Sequence for 1D ^{1}H PFT-NMR



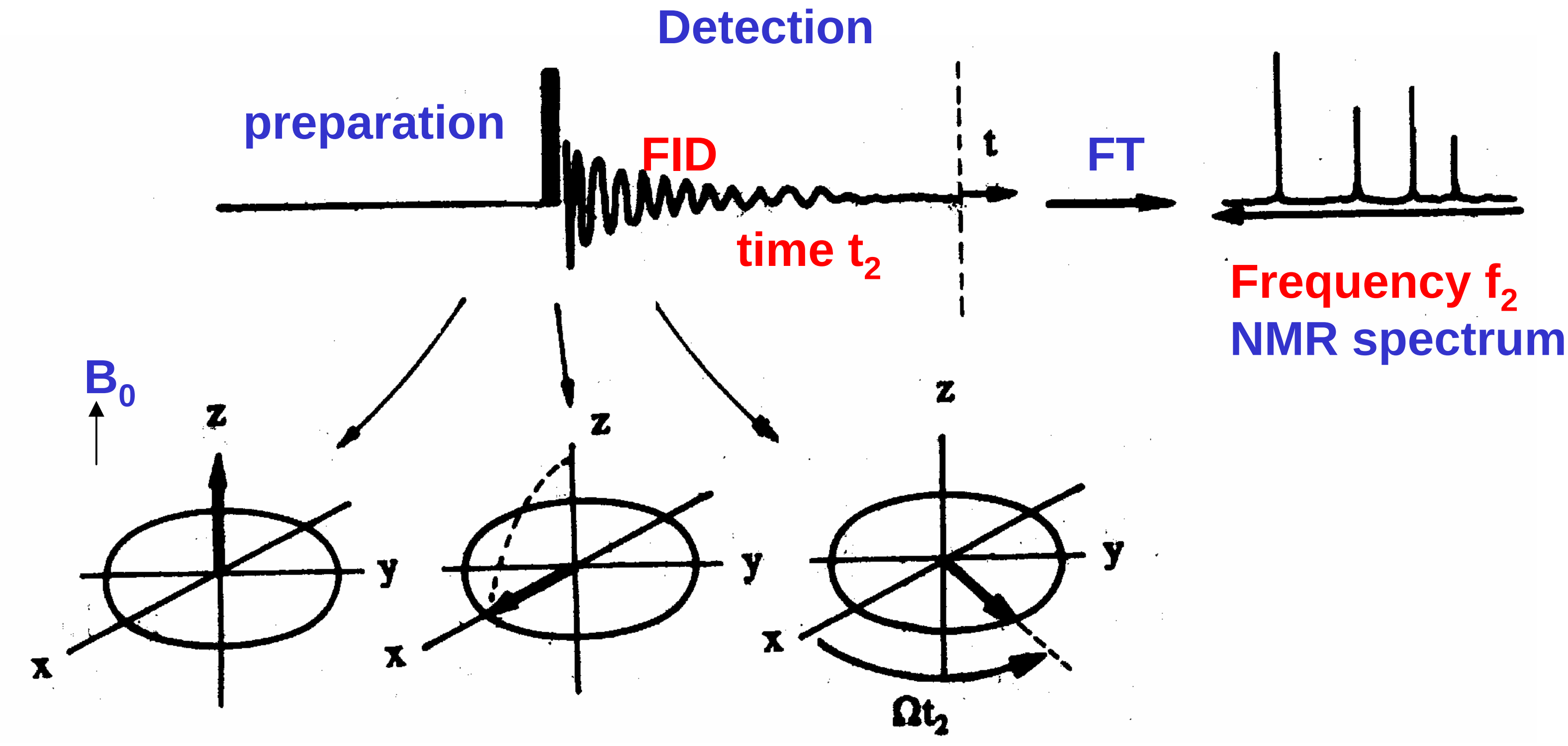
Comparison of Pulse Sequences for 1D ^{1}H and ^{13}C PFT-NMR



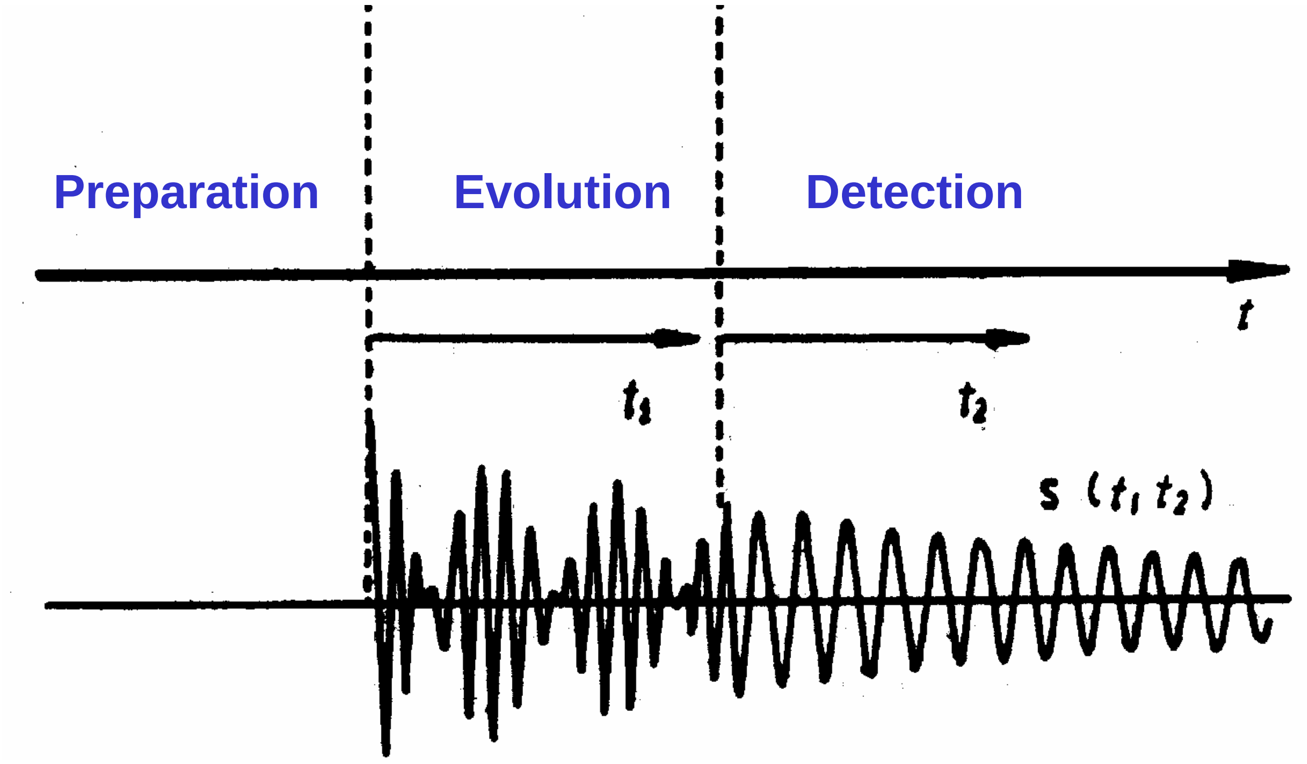
Magnetization, FID and Frequency Spectrum



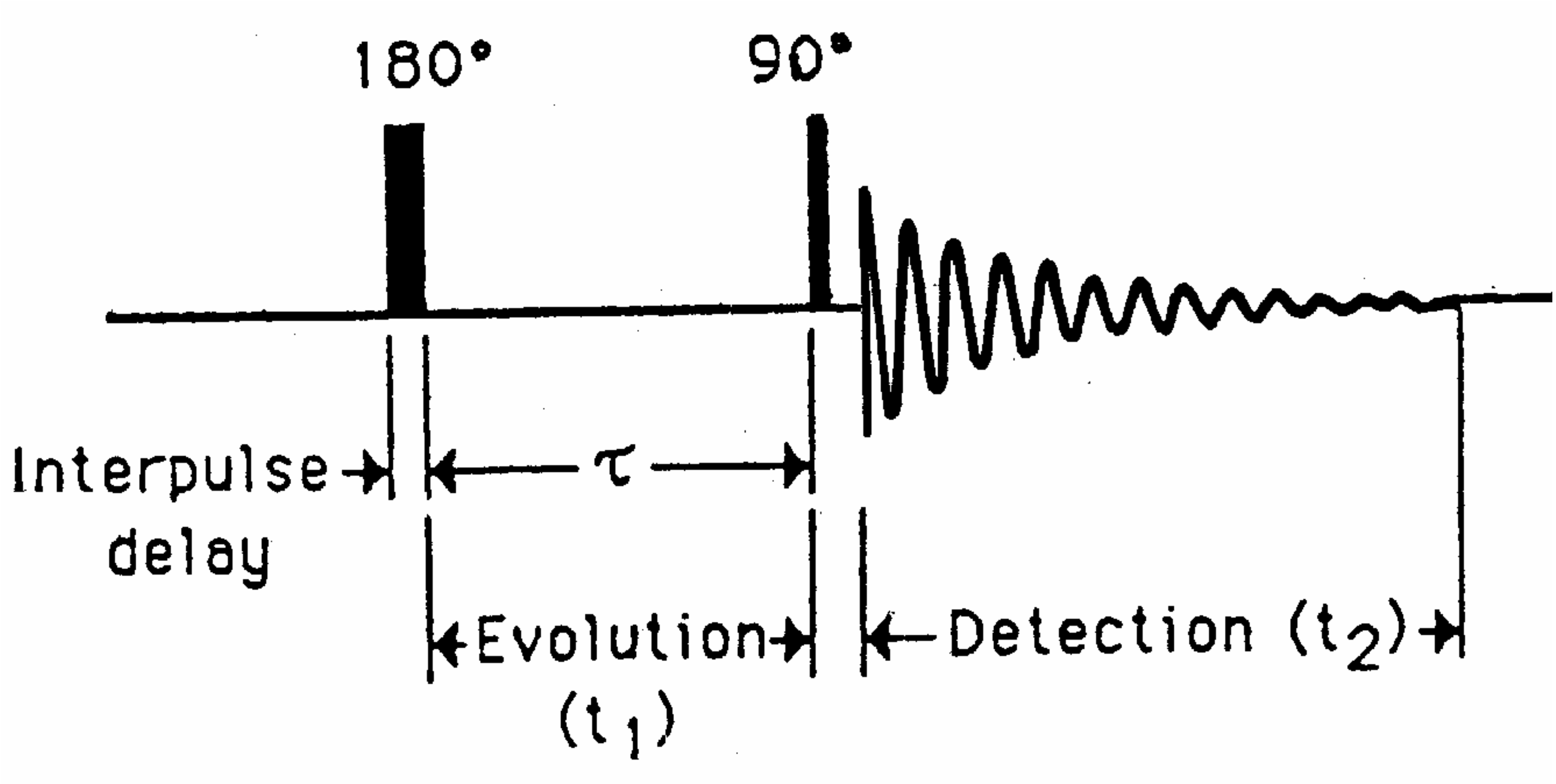
1D PFT-NMR Experiment



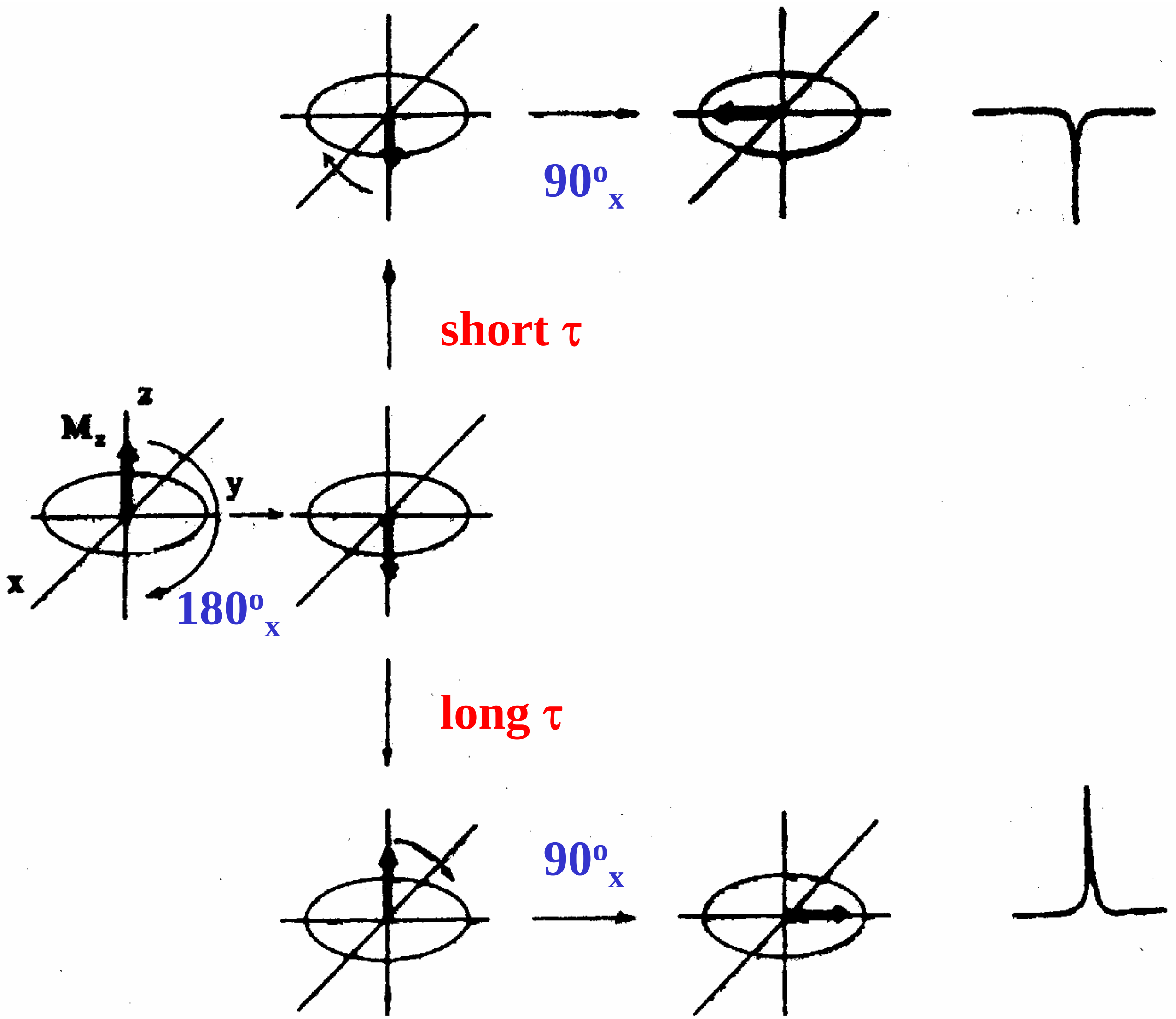
Time-Order of Multiple-pulse NMR Experiments



Inversion Recovery Pulse Sequence



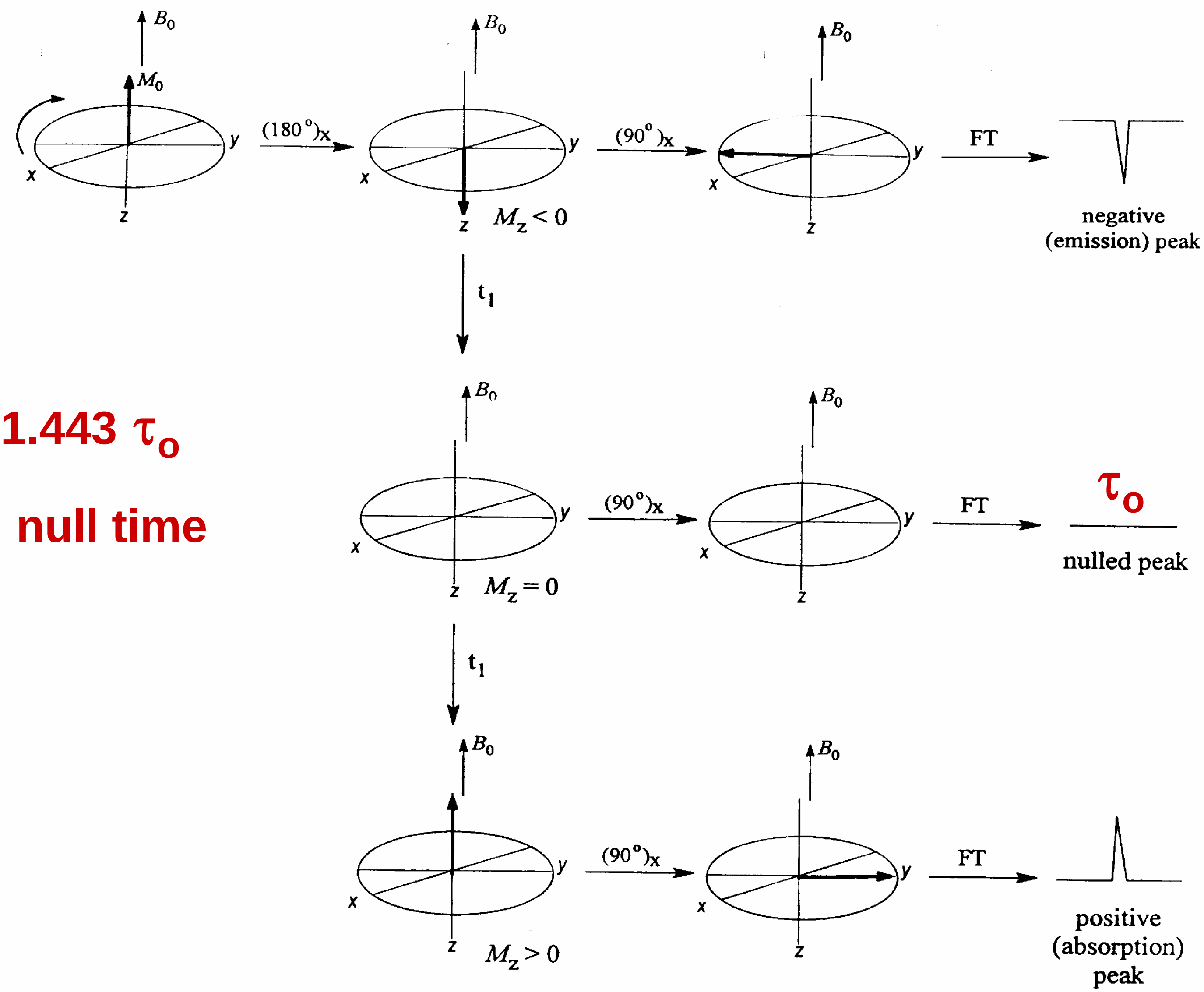
Inversion Recovery Experiment for T_1



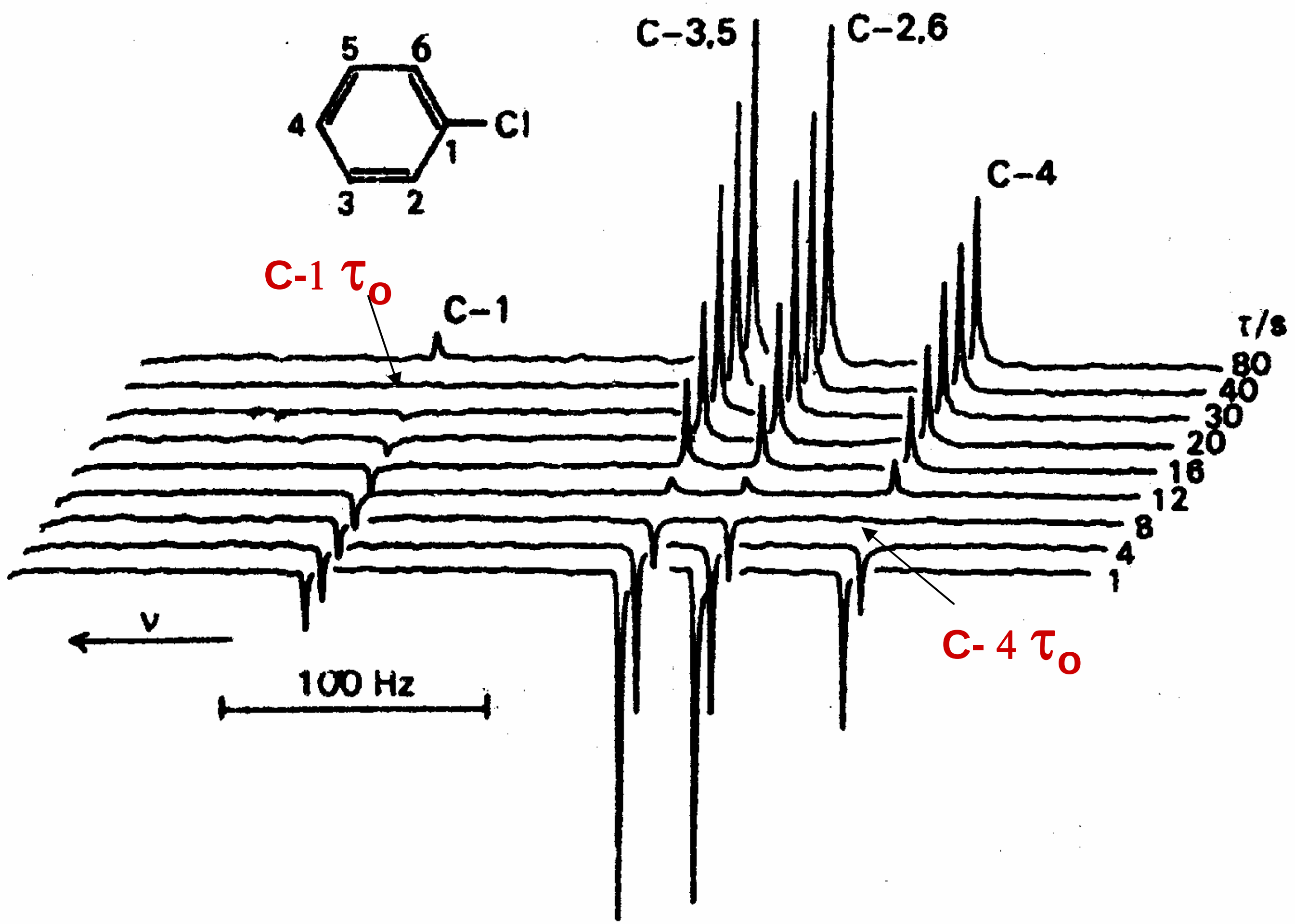
T_1 Null time (τ_o) measurement in Inversion Recovery Experiments

$T_1 = 1.443\ \tau_o$

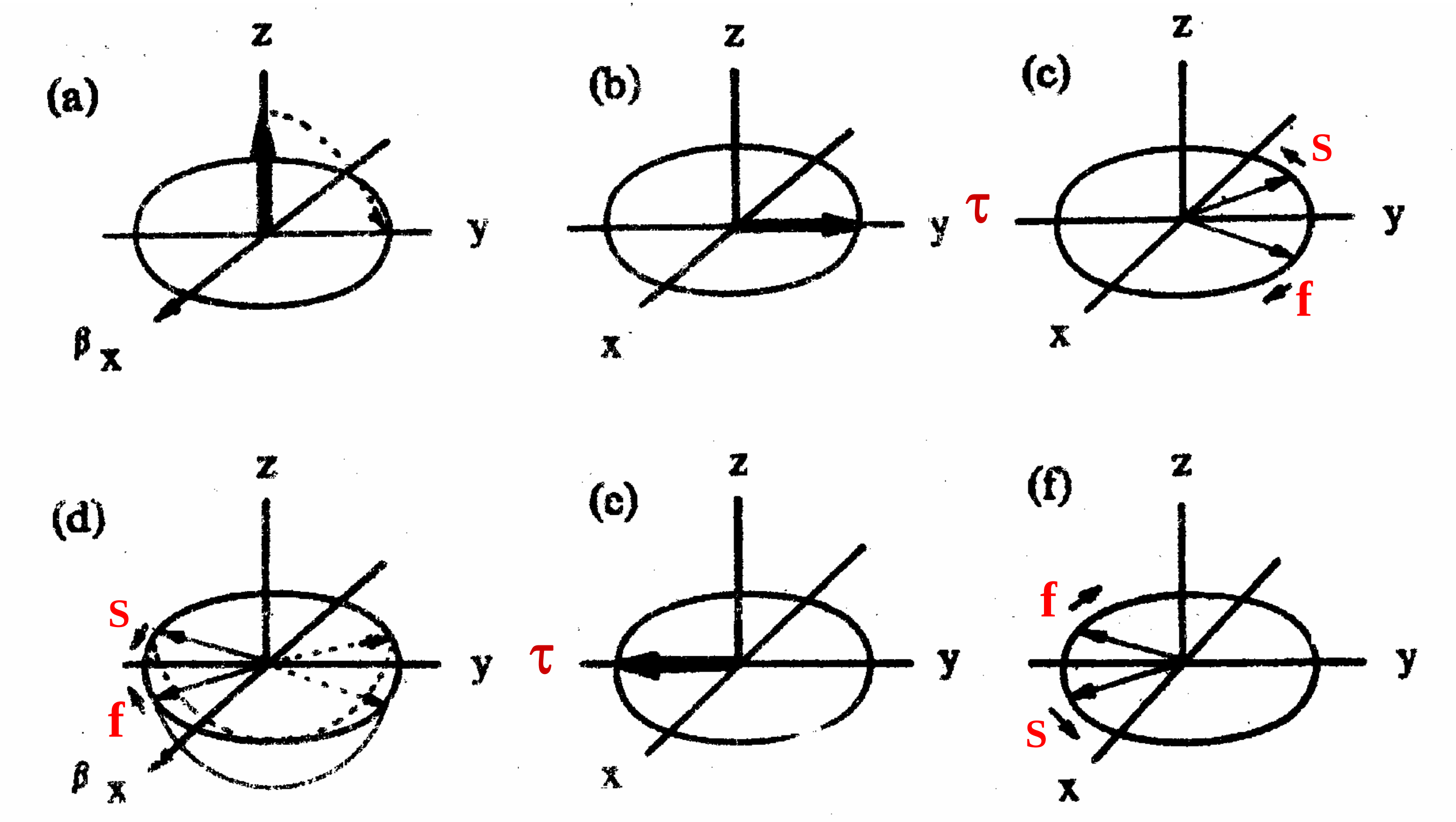
τ_o : null time



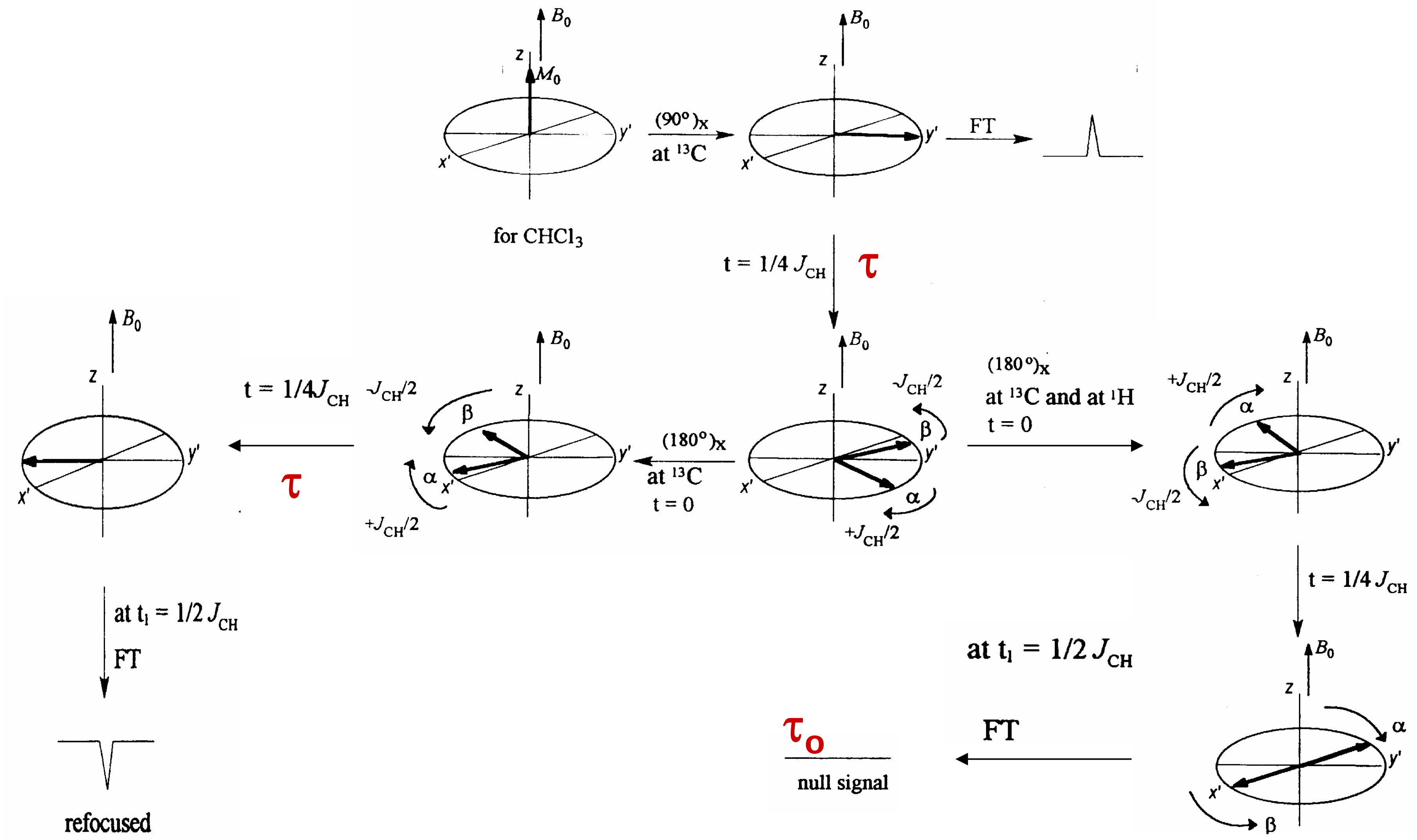
^{13}C T_1 Measurement by Inversion Recovery Experiments



Spin Echo Pulse Sequence

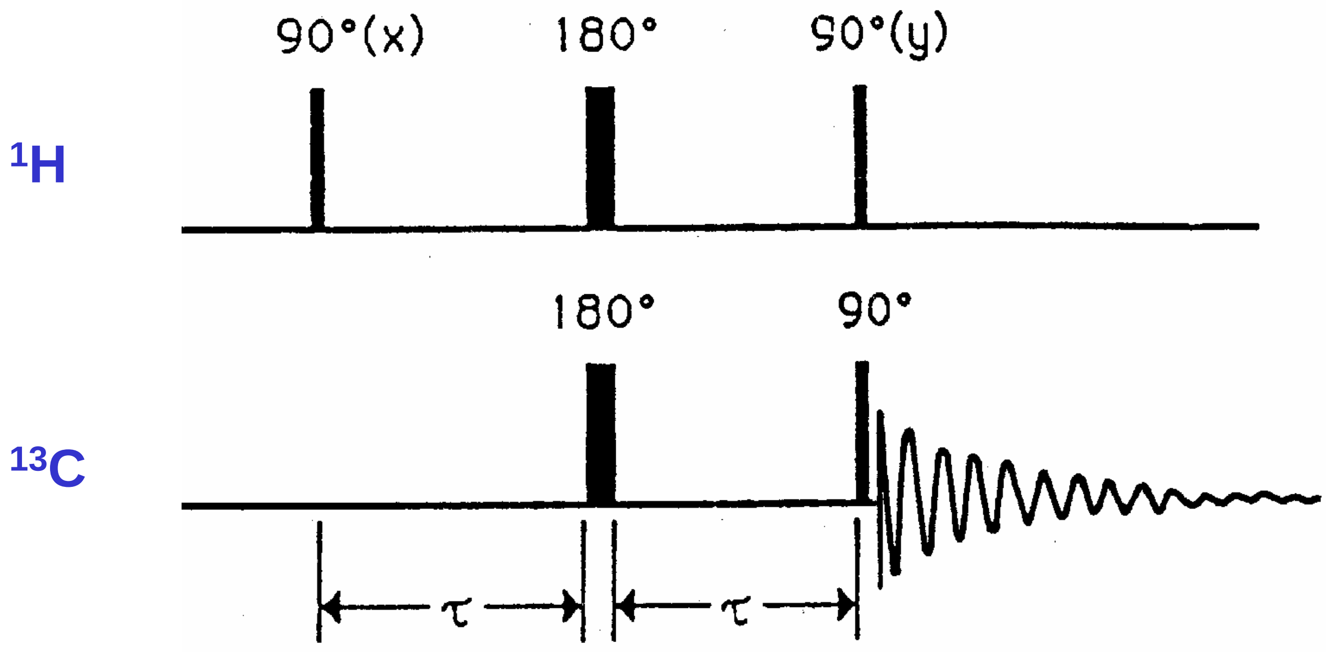


T_2 Null Time Measurement in Spin-Echo Experiments

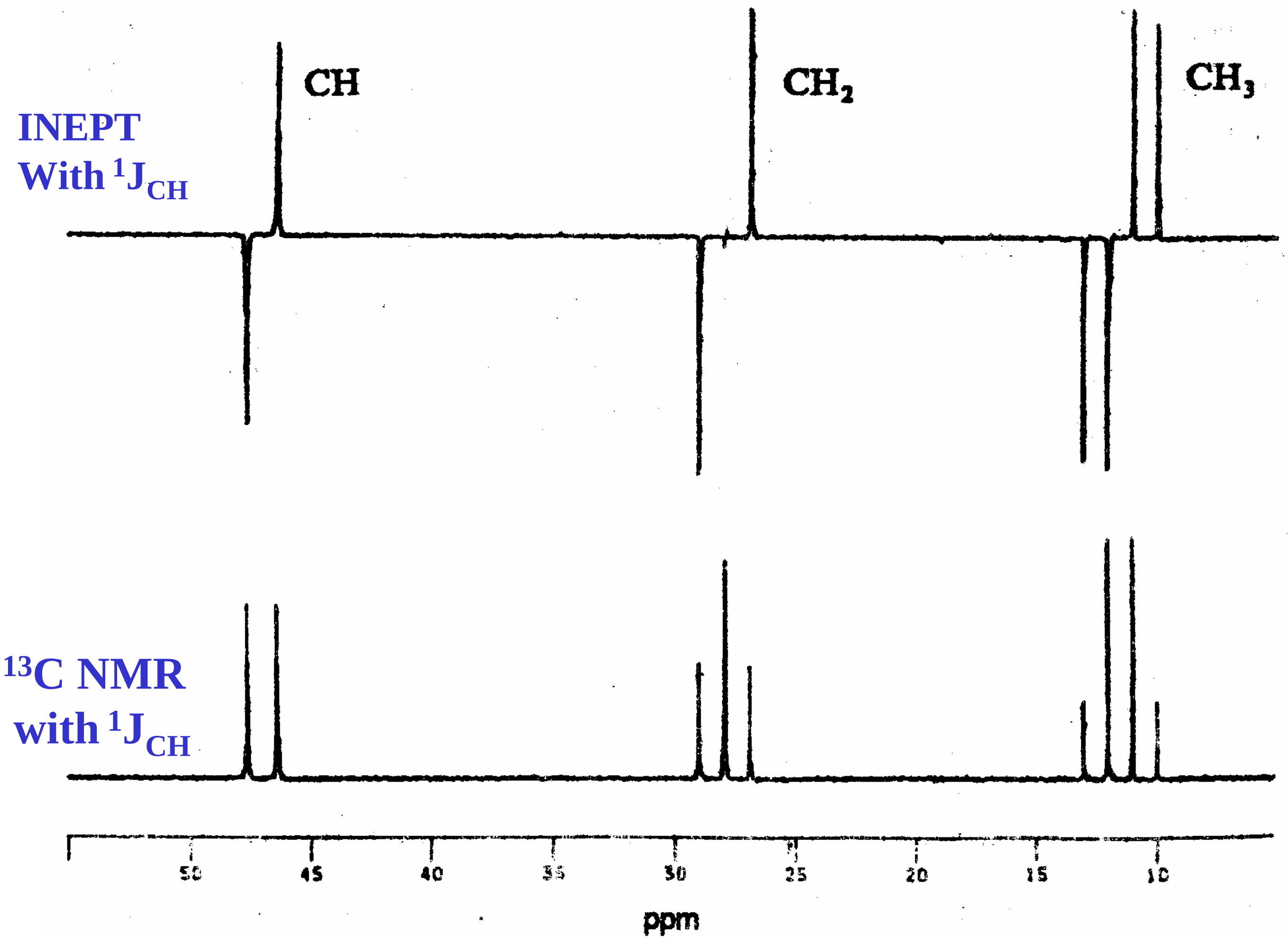


Polarization transfer experiments

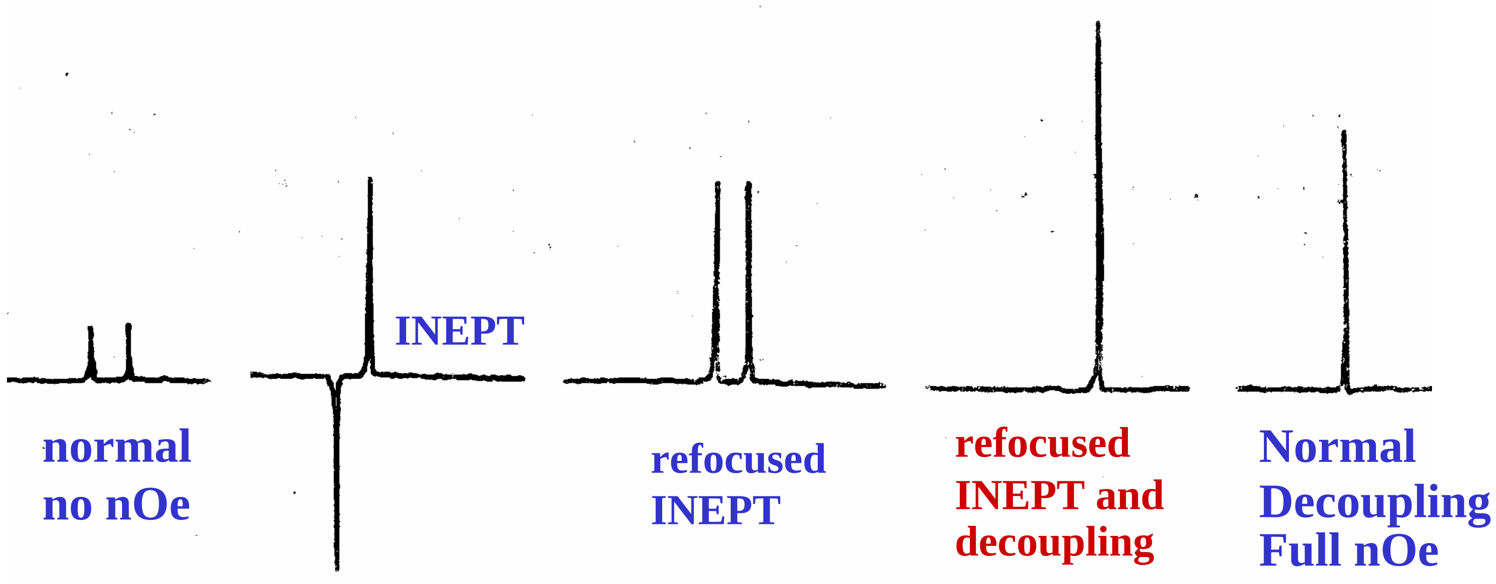
INEPT(Insensitive Nuclei Enhanced by Polarization Transfer)



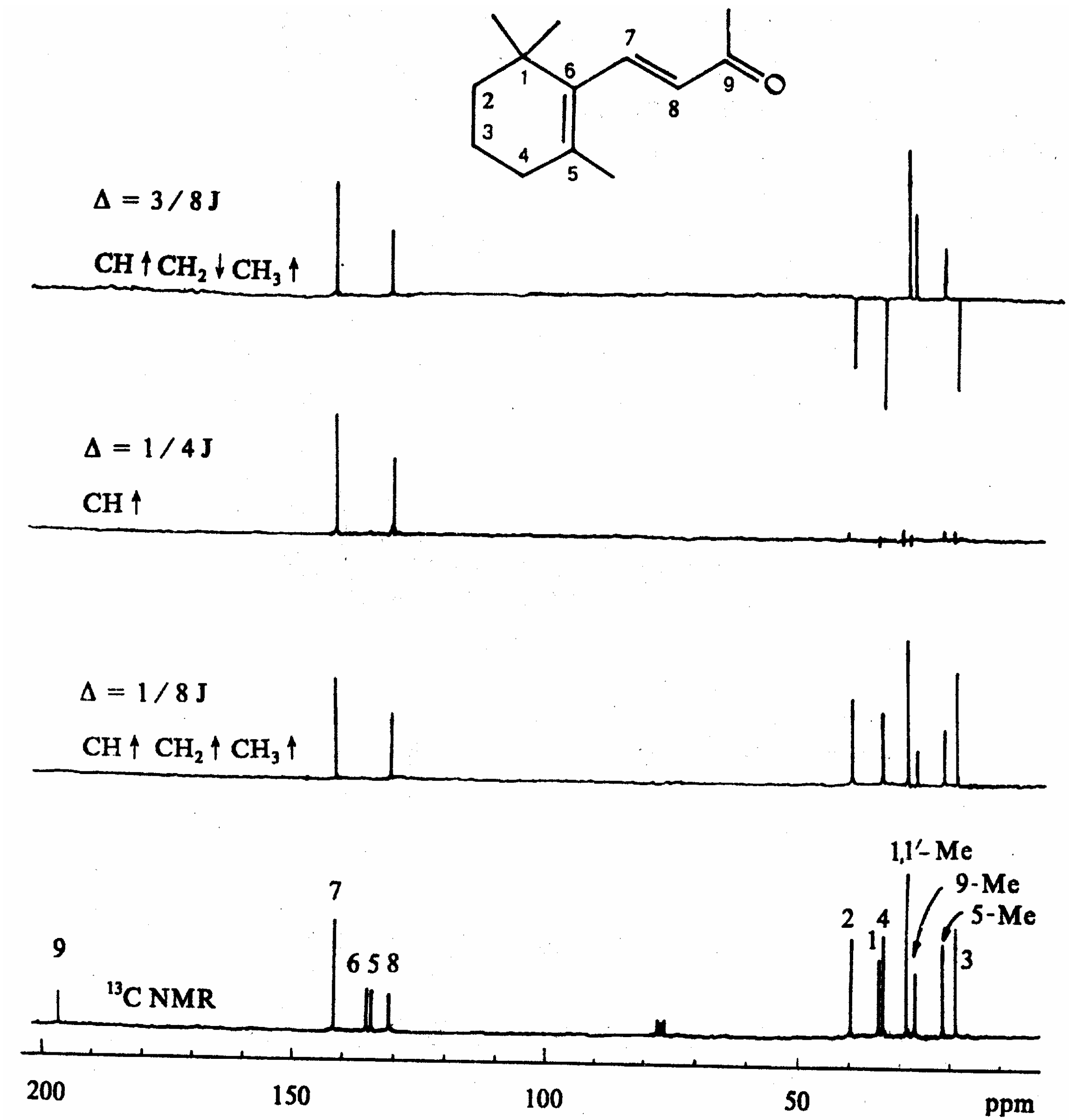
Characteristic Coupled INEPT Spectral Patterns



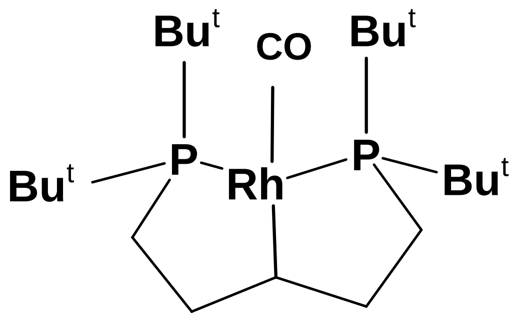
Permutations on the INEPT Spectrum of $CHCl_3$

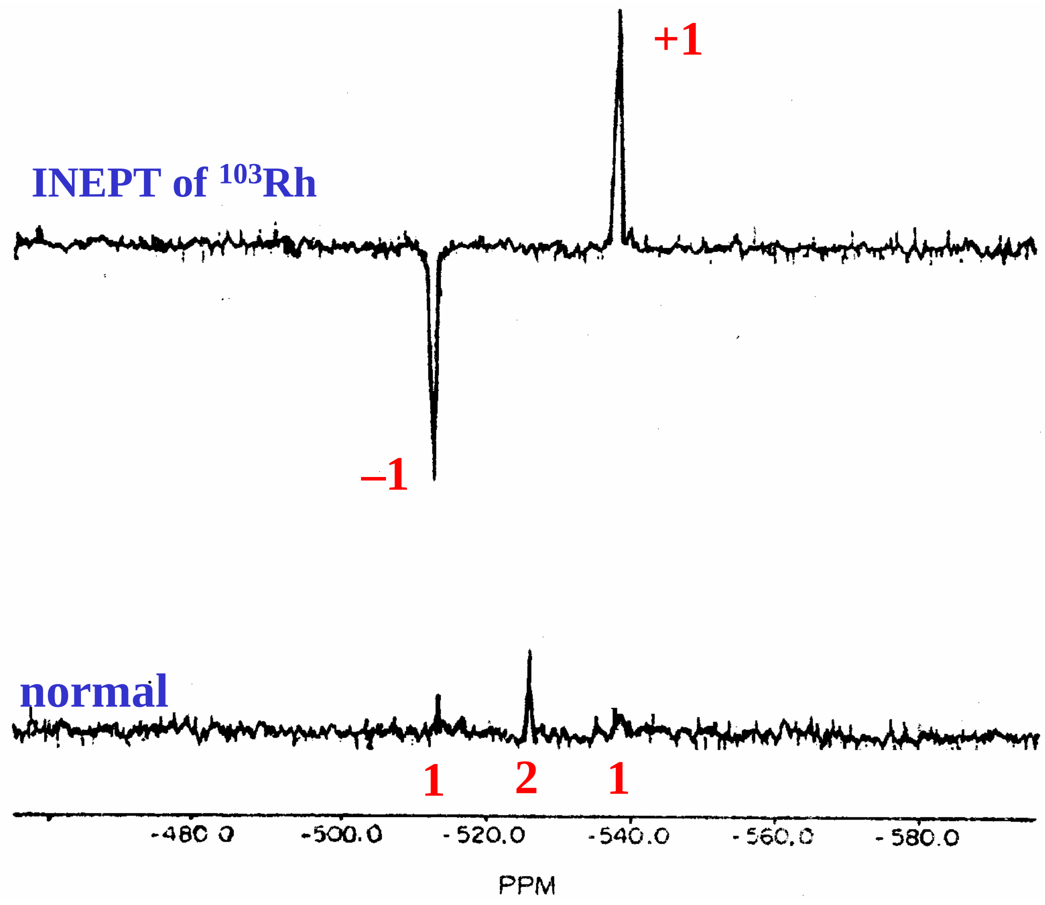


INEPT Spectra of β-Ionone



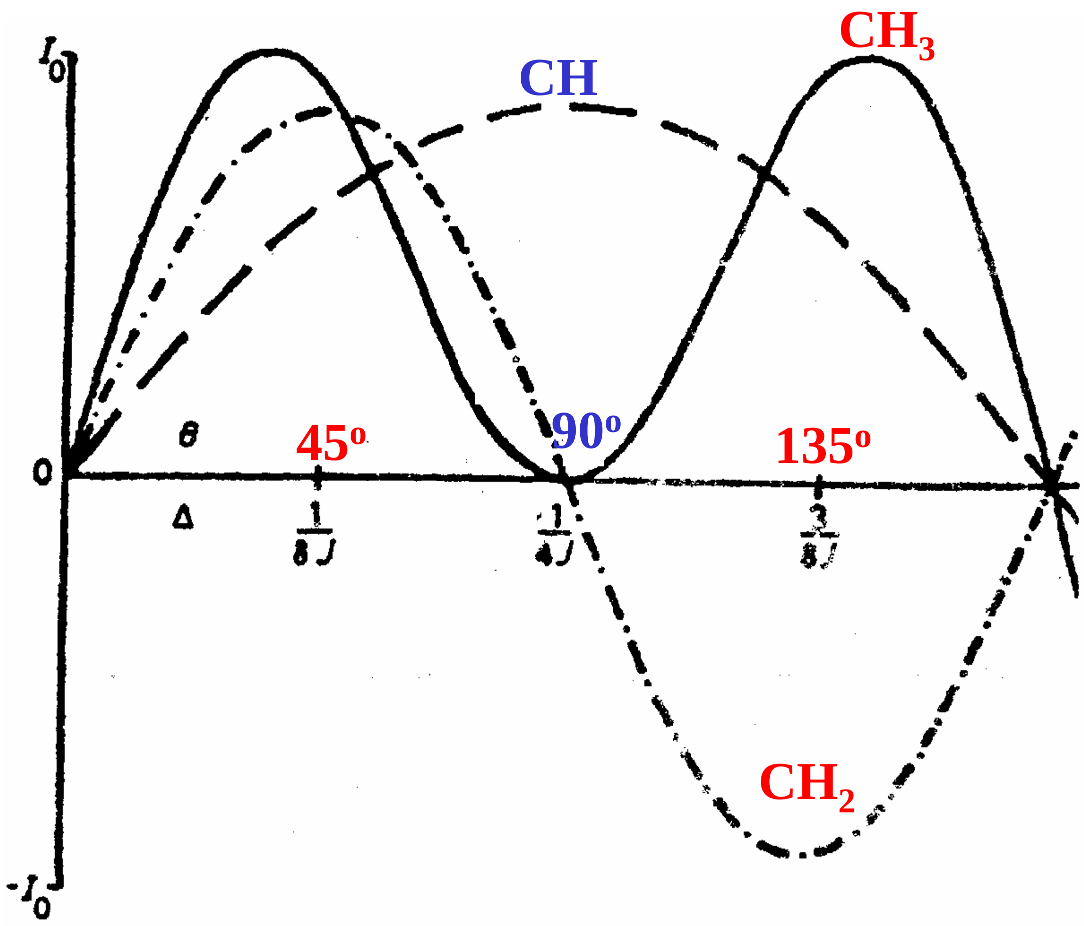
INEPT Enhancement of ^{103}Rh by Polarization Transfer from ^{31}P



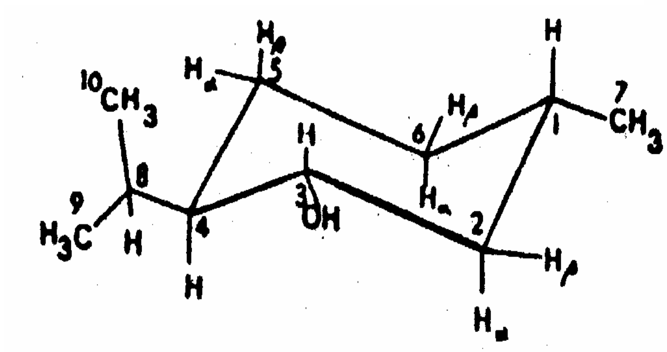


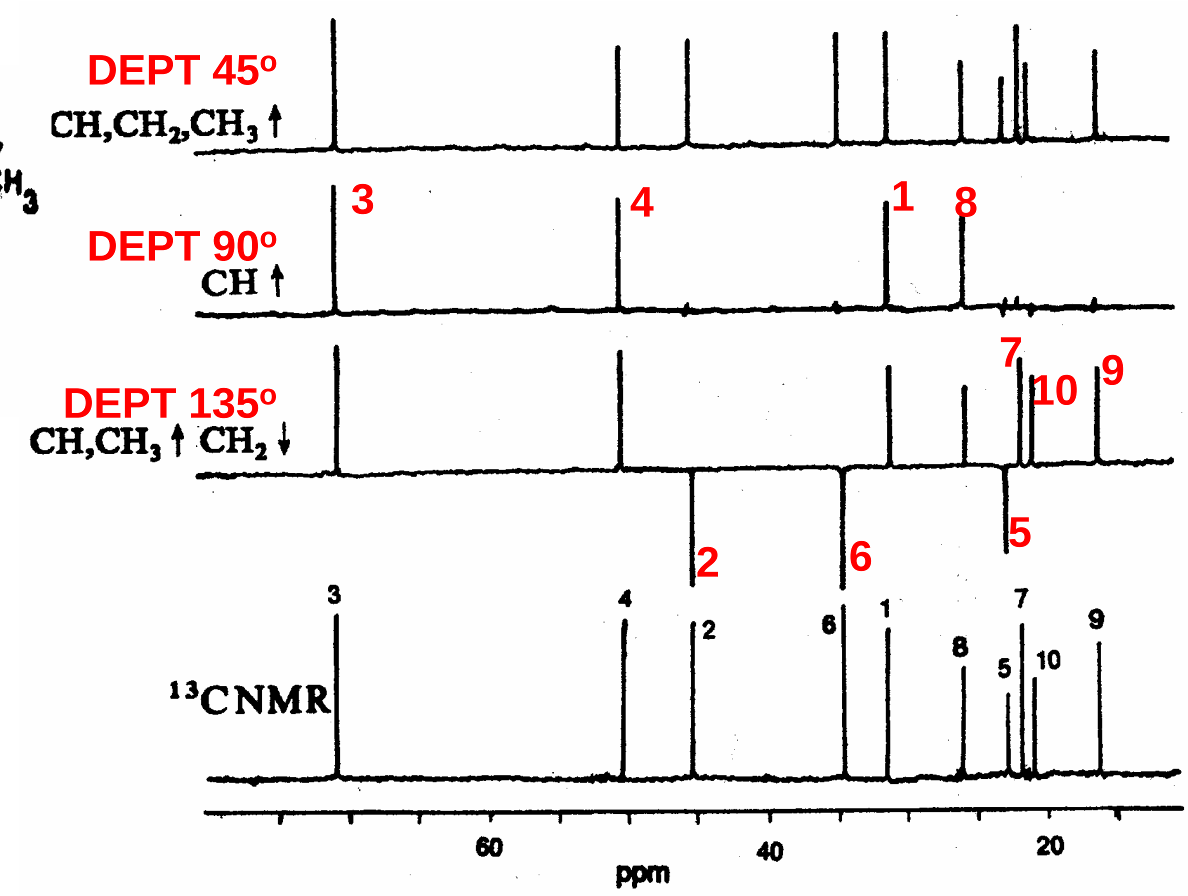
The Relationship between Signal Intensities and the Pulse Angle (θ) of DEPT

(Distortionless Enhancement by Polarization Transfer)

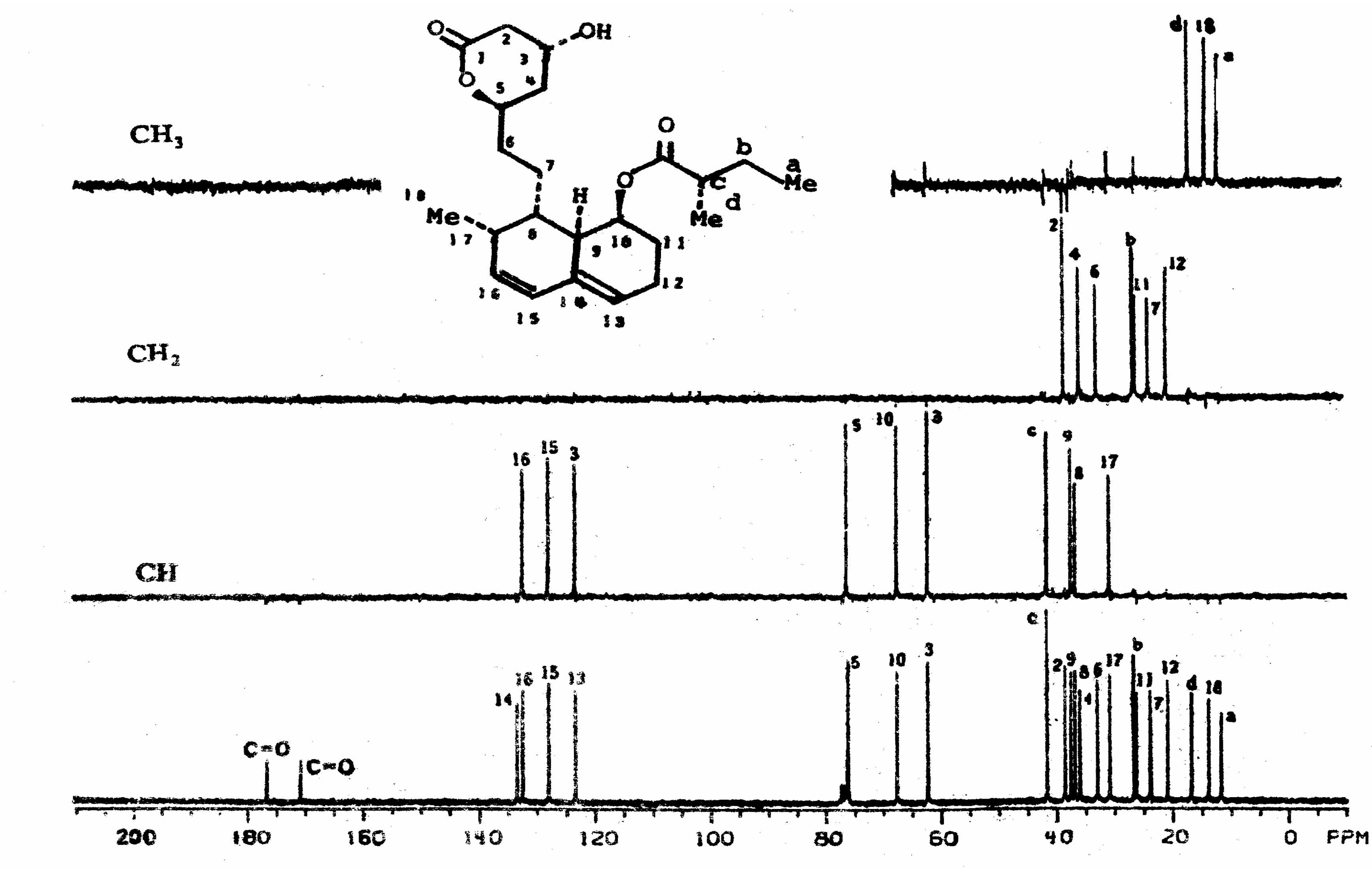


DEPT Spectra of Menthol



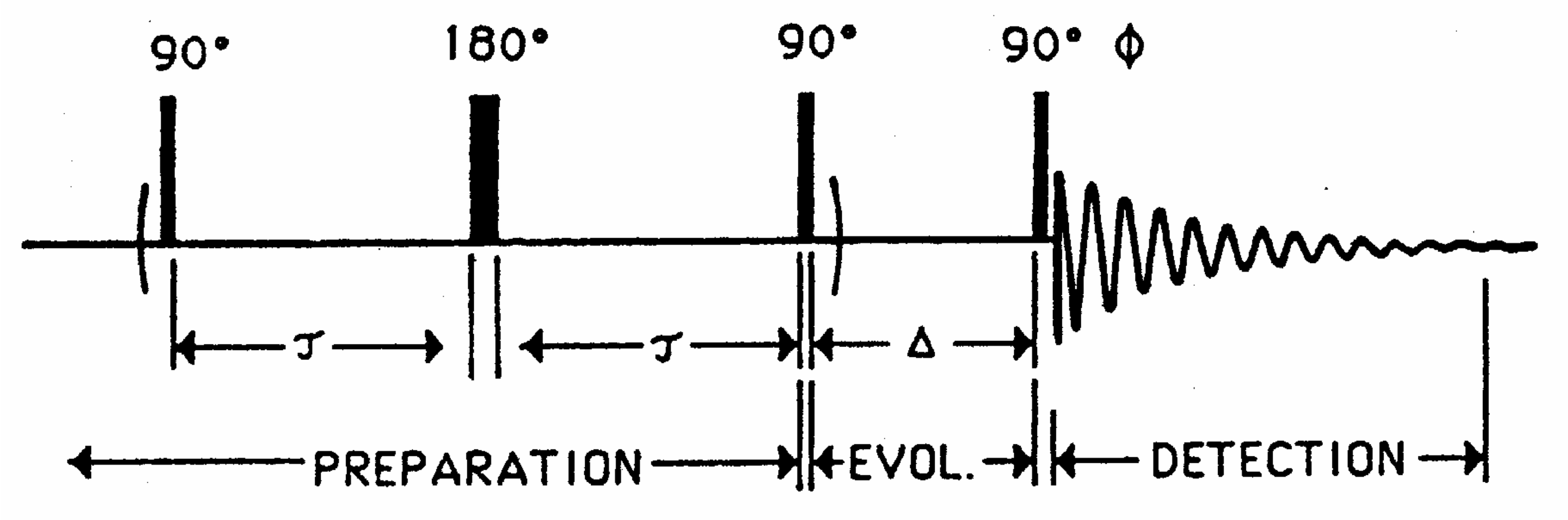


Editing DEPT Spectra

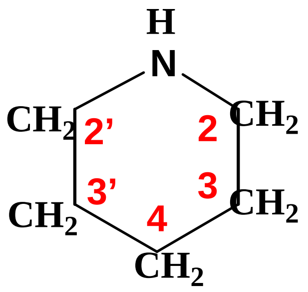


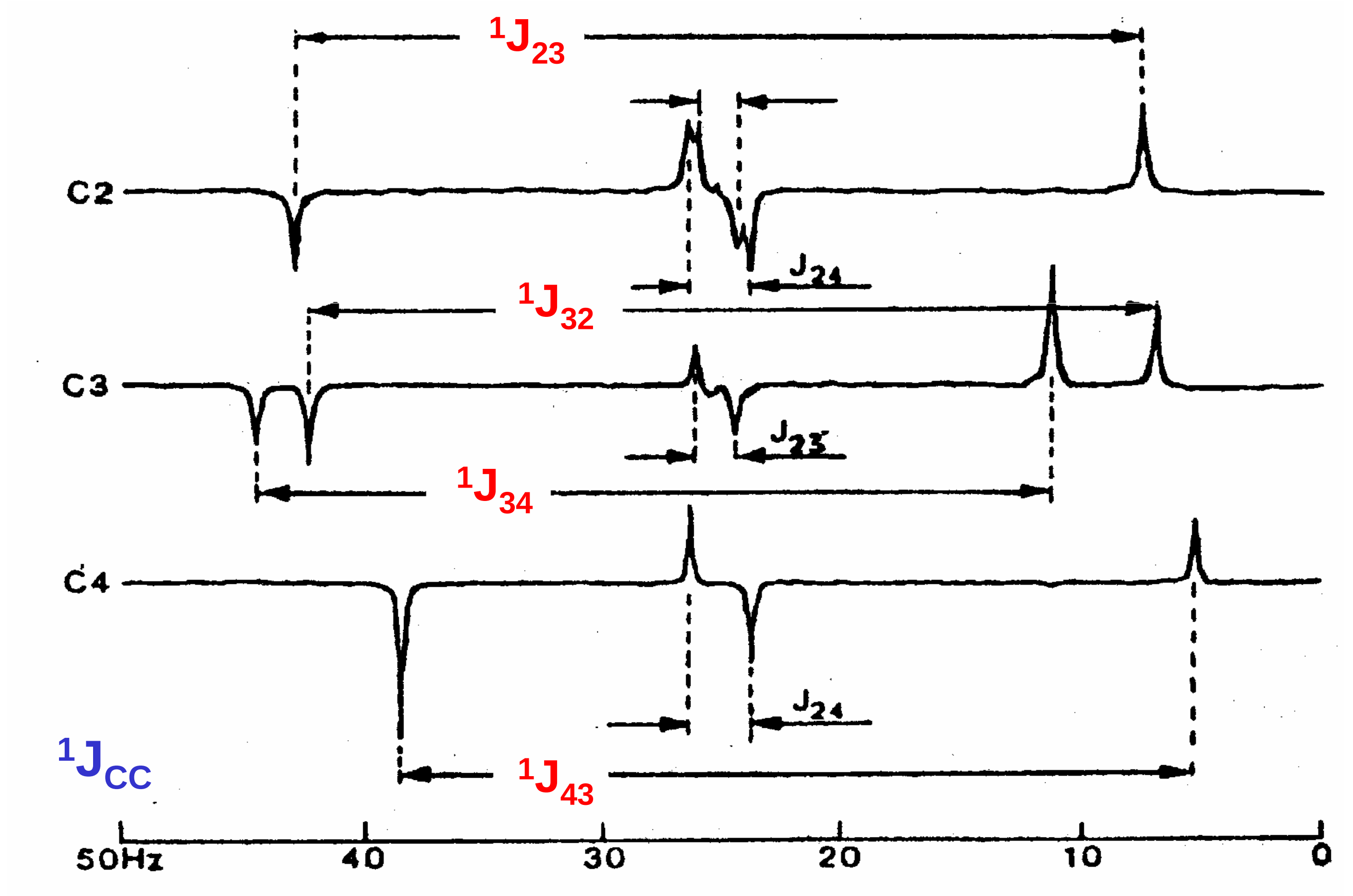
1D pulse sequence of INADEQUATE ($^1J_{CC}$)

(Incredible Natural Abundance Double Quantum Transfer Experiment)

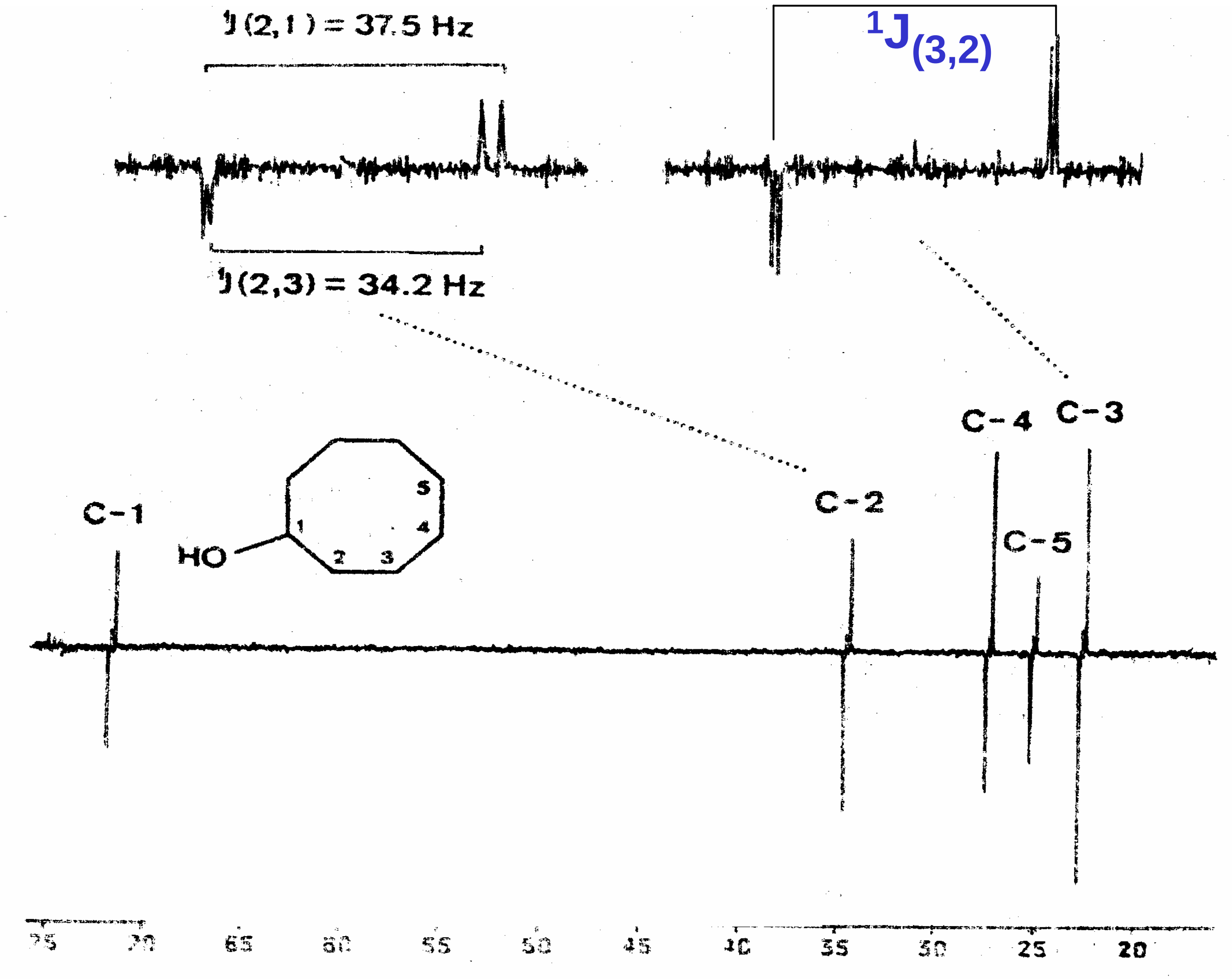


1D INADEQUATE Spectra of Piperidine

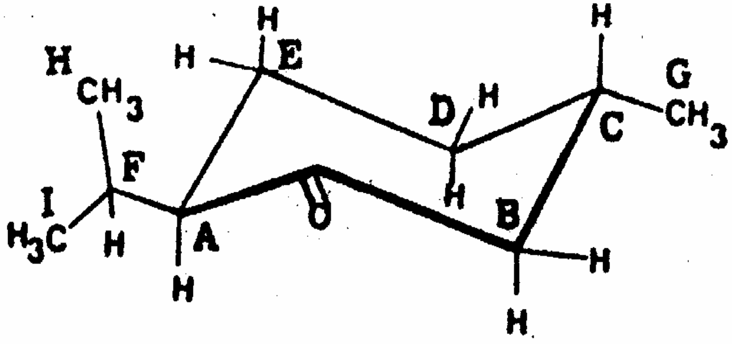


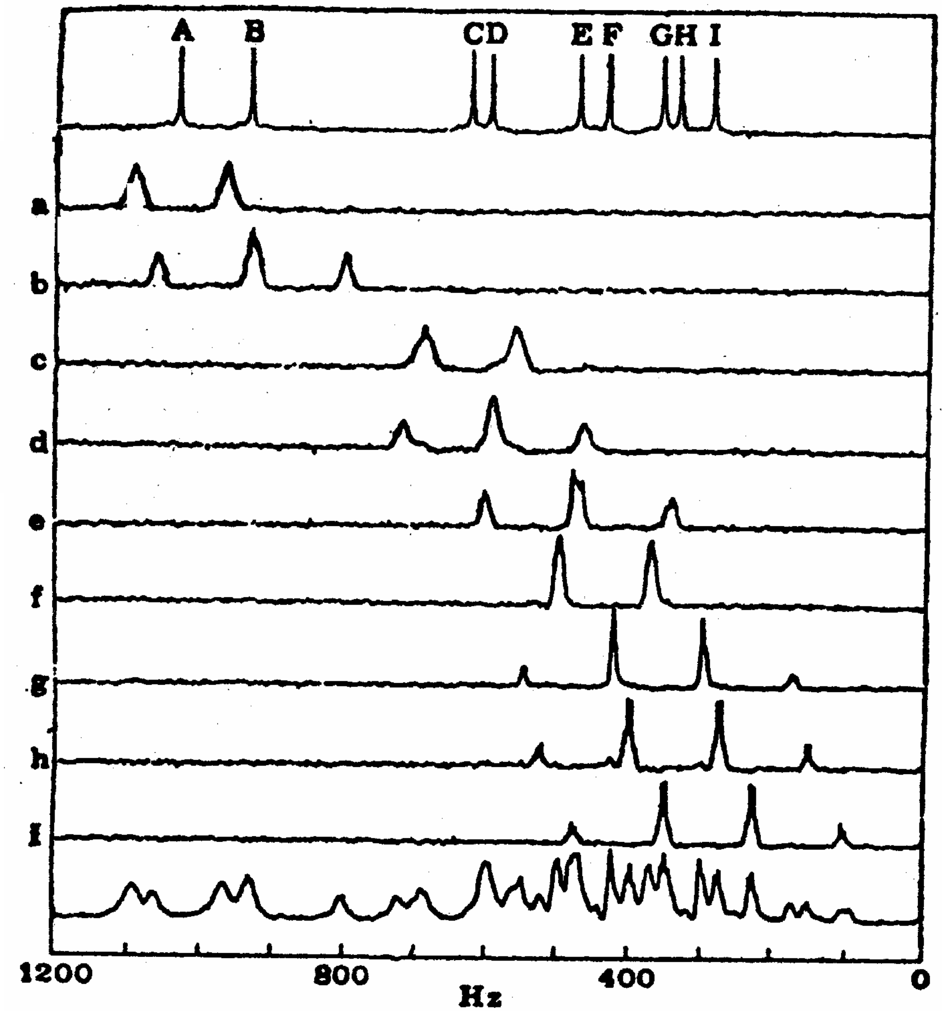


1D INADEQUATE Spectrum of Cyclooctanol

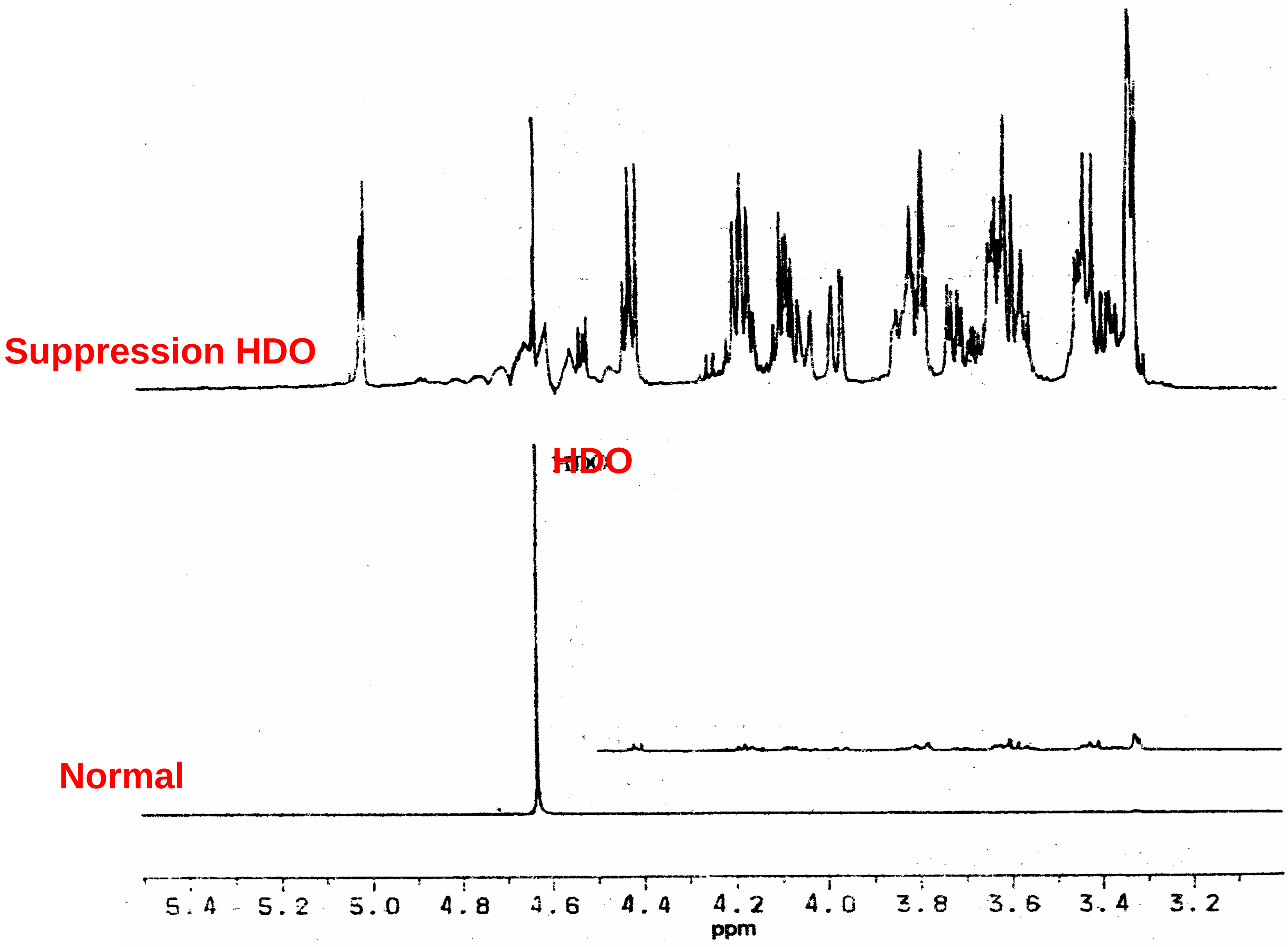


Selective Excitation and Suppression
DANTE experiment
(Delays Alternating with Nutations for Tailored Excitation)

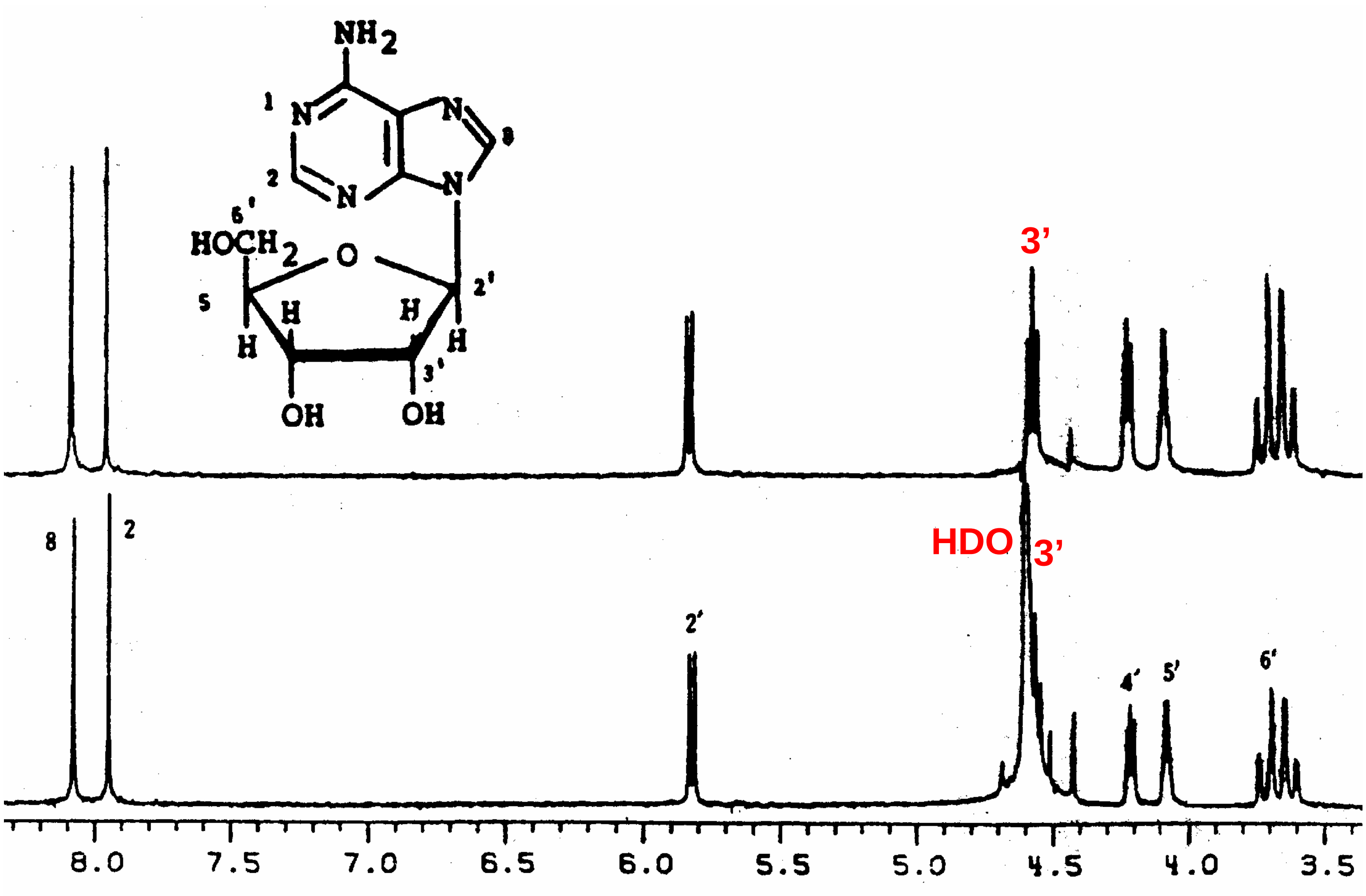




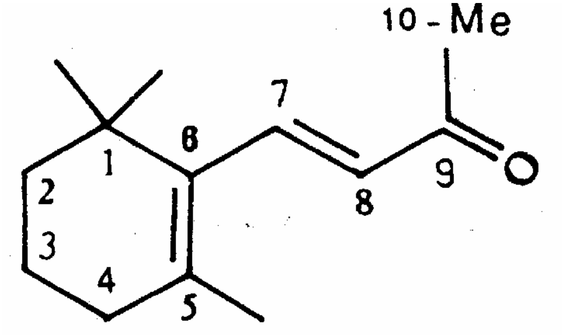
Peak Suppression: Suppression of the Peak of HDO by Pre-saturation

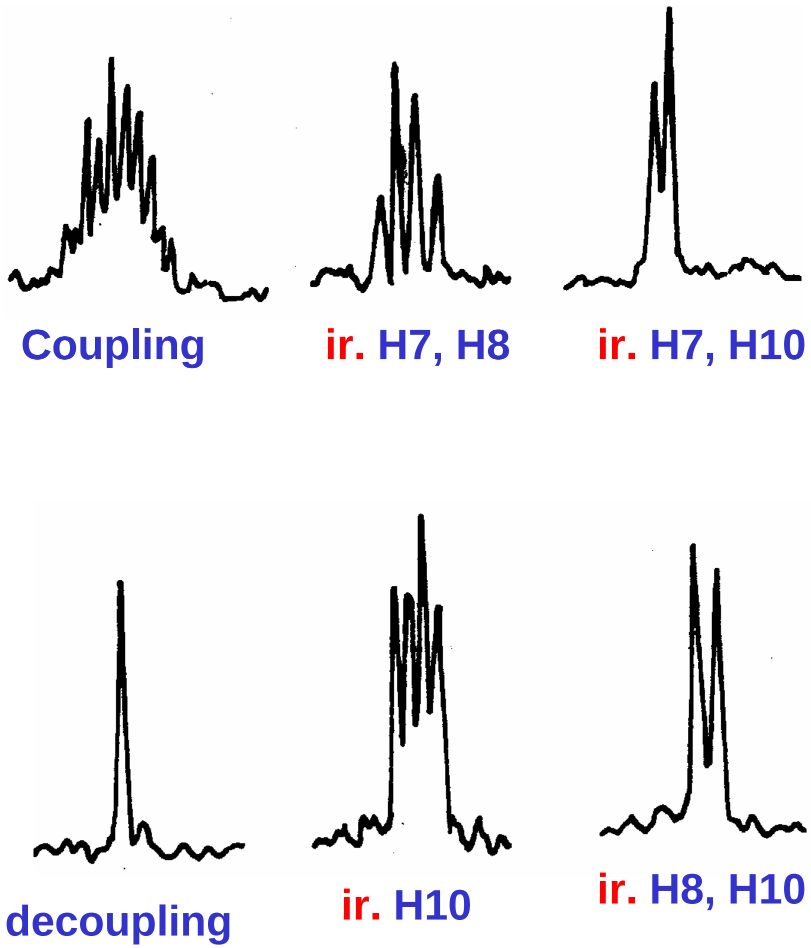


Peak Suppression: WEFT Experiments (Water Eliminated Fourier Transform)

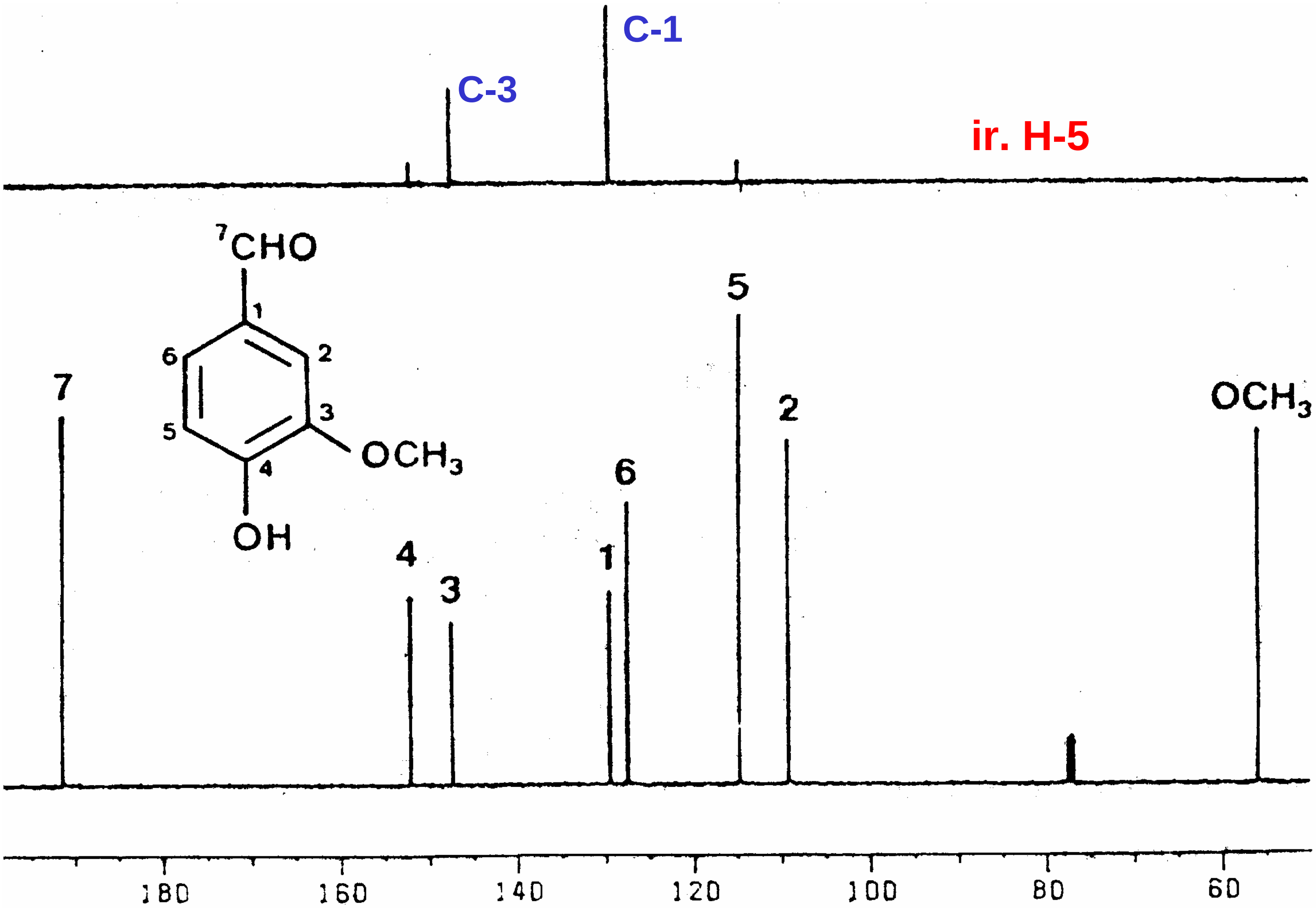


Long-range Selective Proton Decoupling C-9 Spectrum of β-Ionone

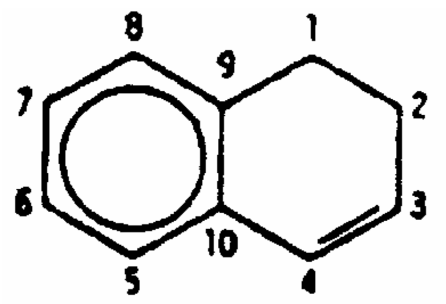


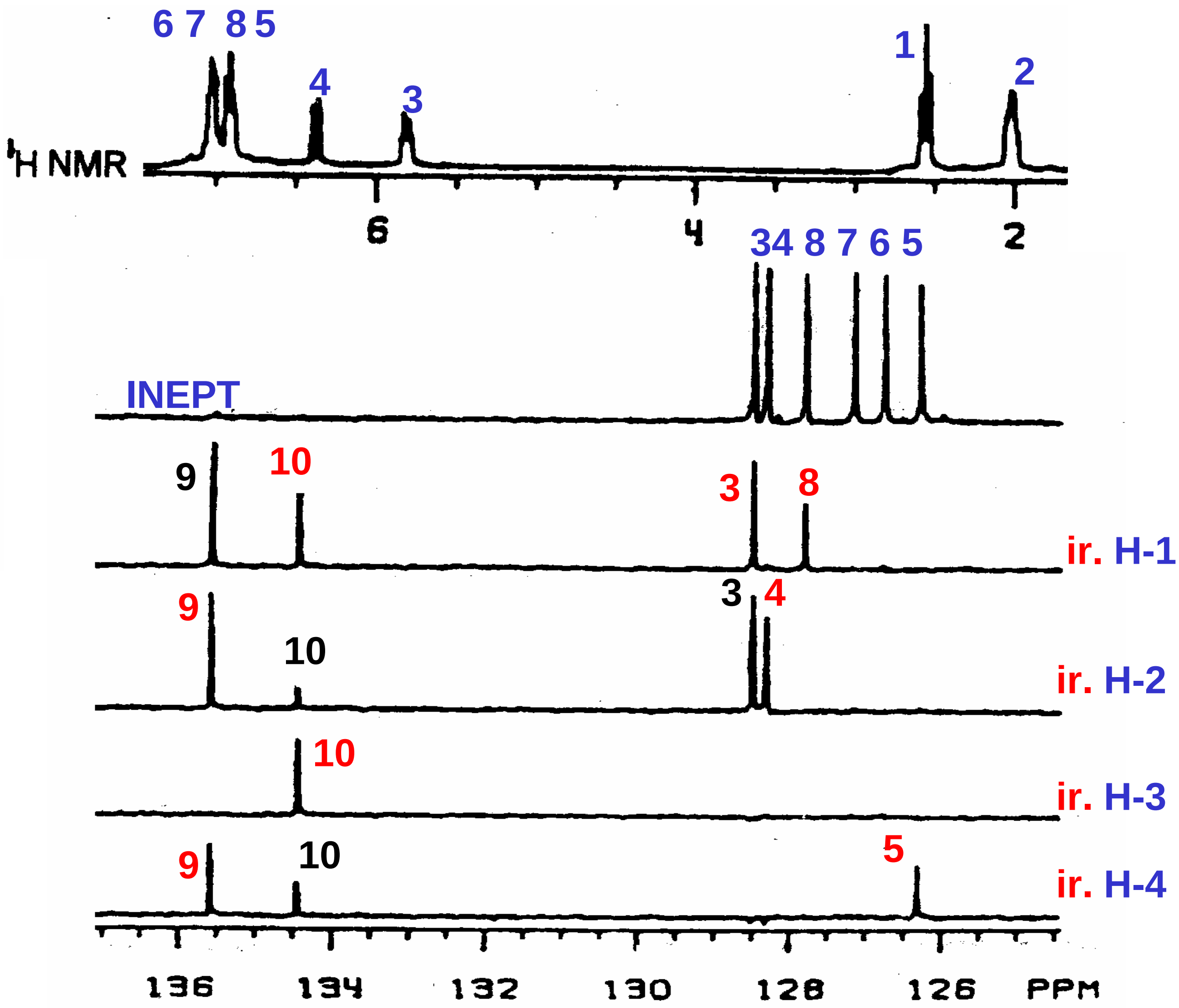


Selective Excitation INEPT Experiment of Vanillin

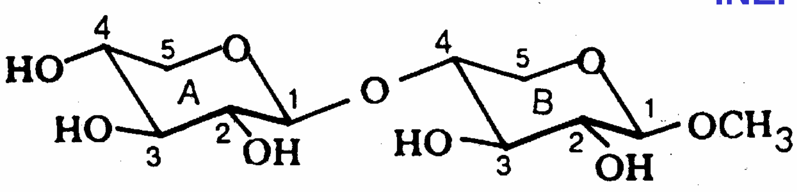


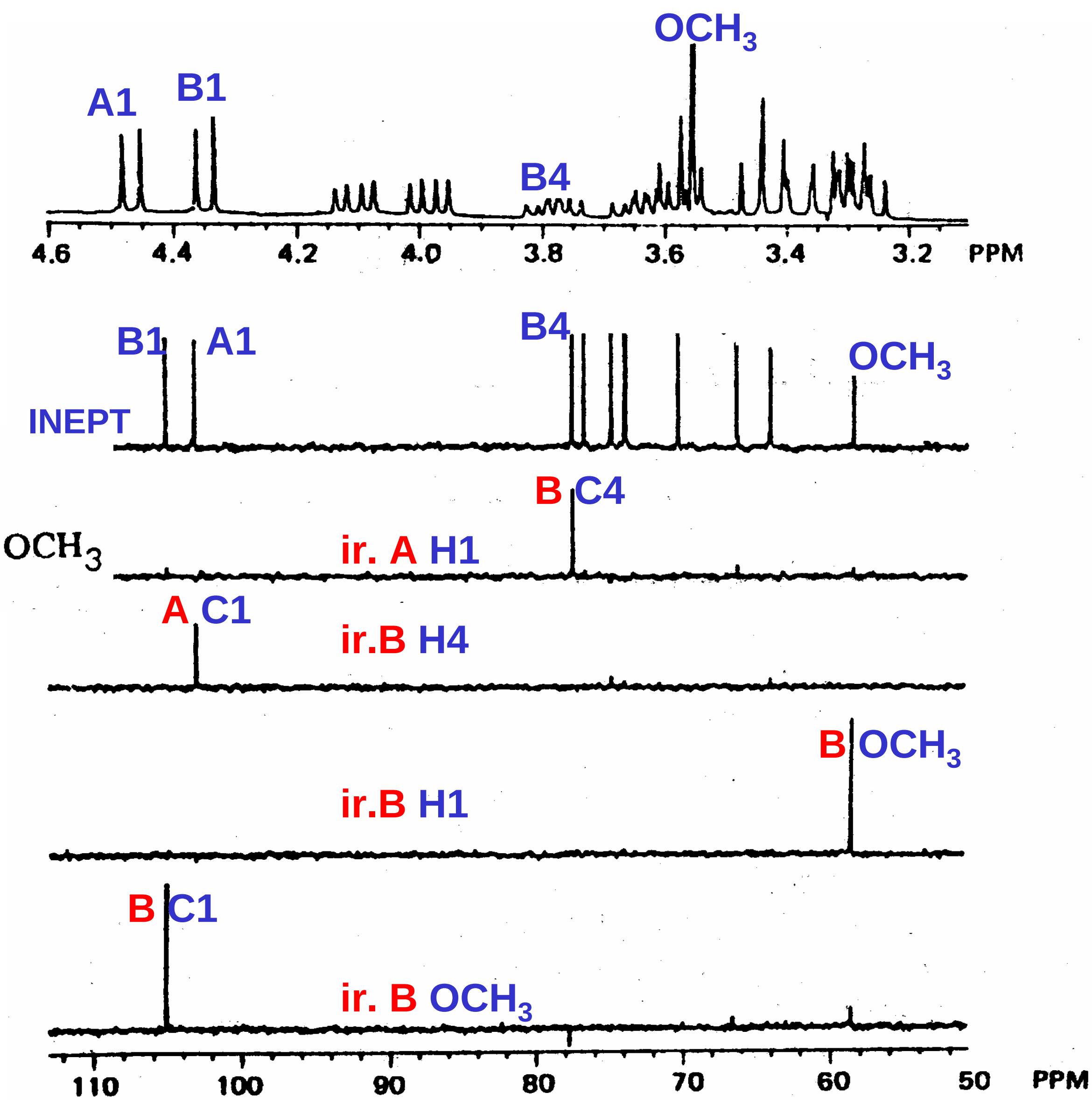
Selective Excitation INEPT Experiments





Selective Excitation INEPT Experiments



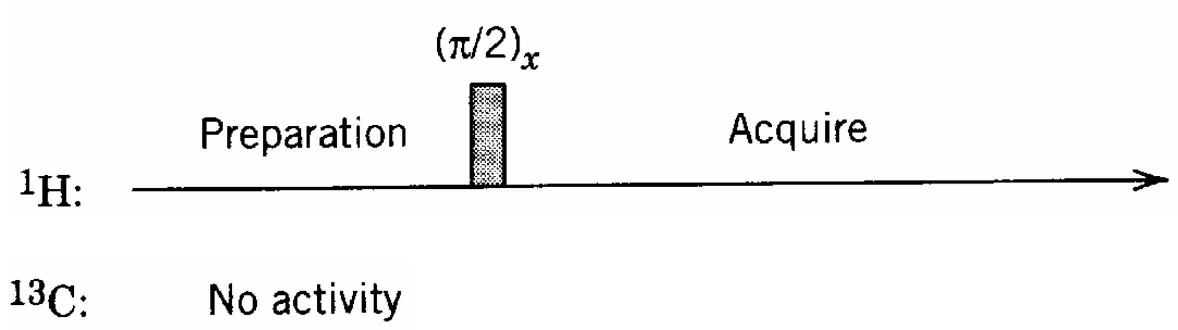


Chapter 7

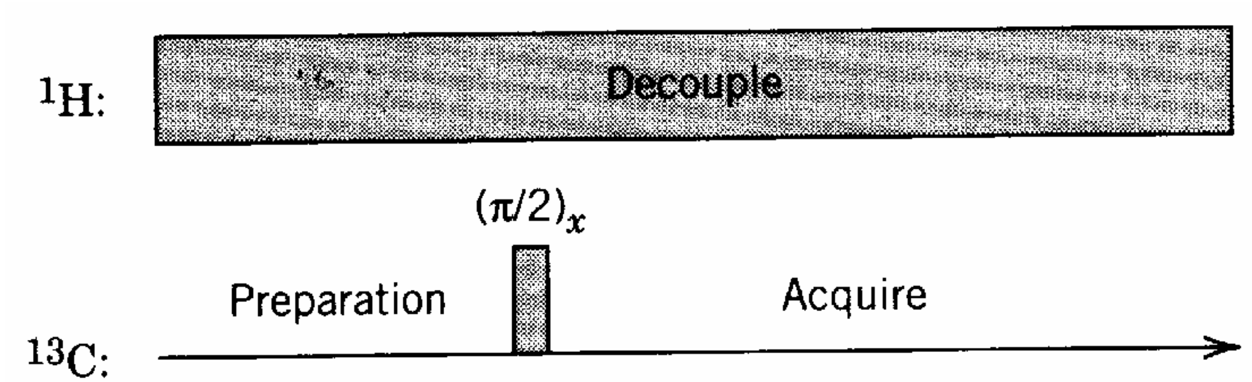
2D Correlation NMR Spectroscopy

Principles of 1D and 2D NMR Spectroscopy

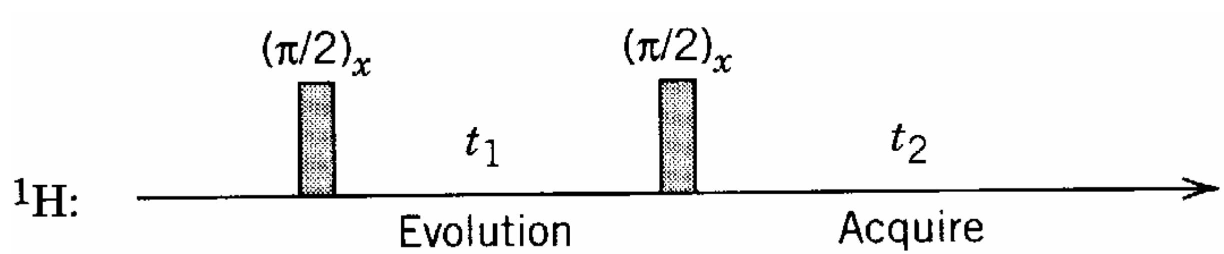
^{1}H NMR



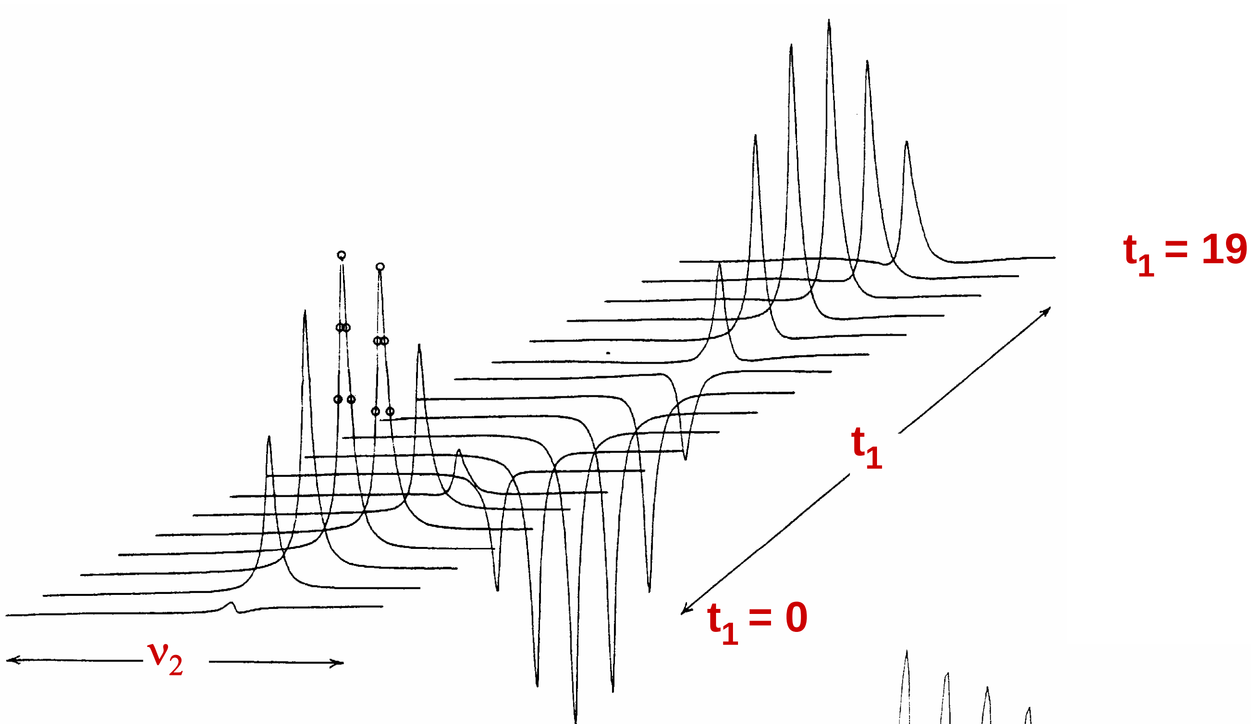
^{13}C NMR

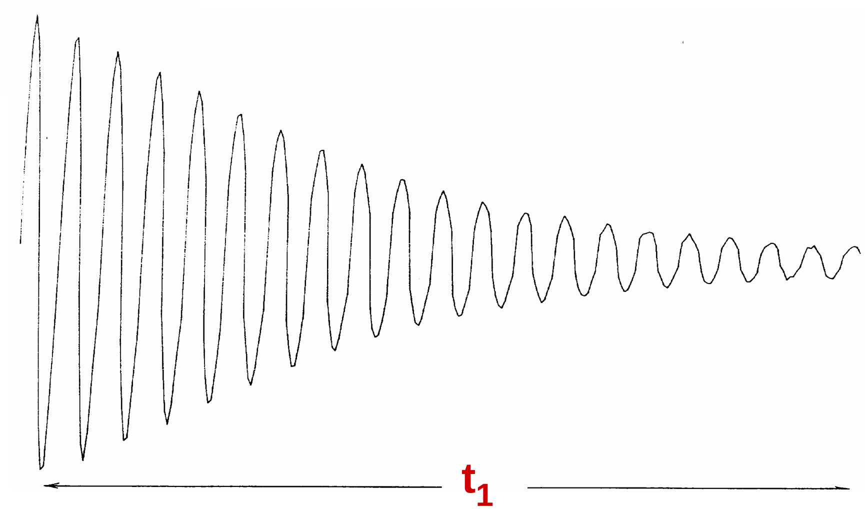


2D NMR
H,H COSY

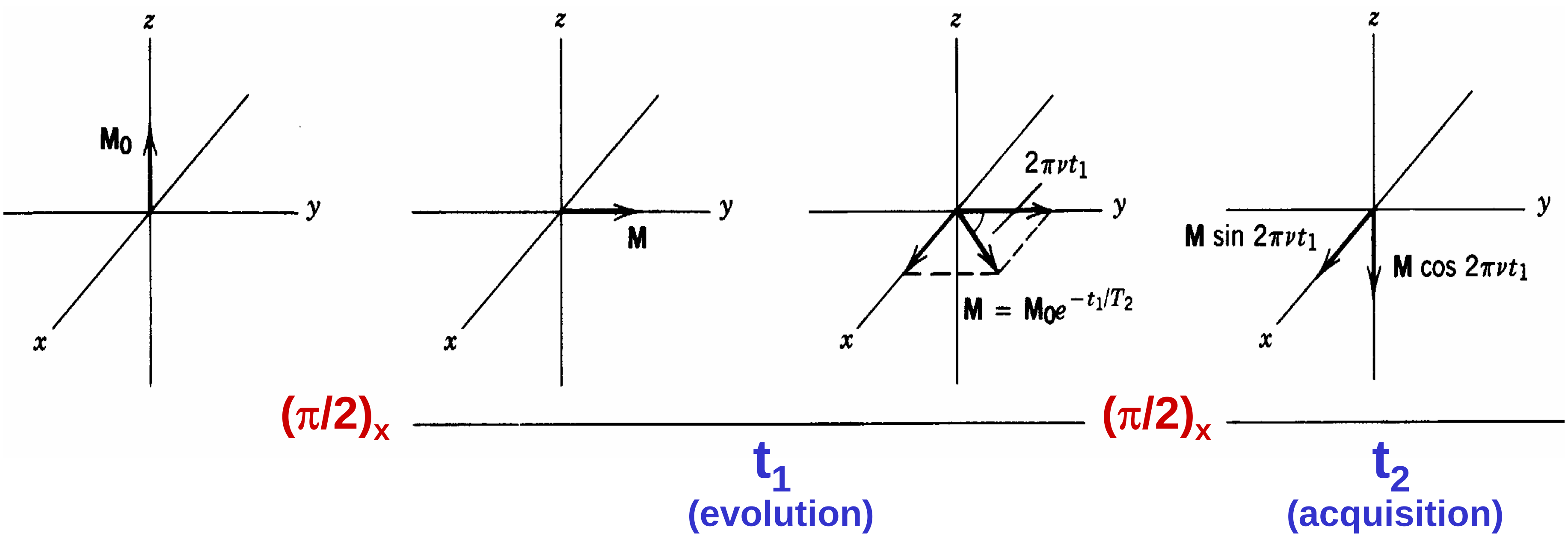


Principles of 2D NMR Spectroscopy

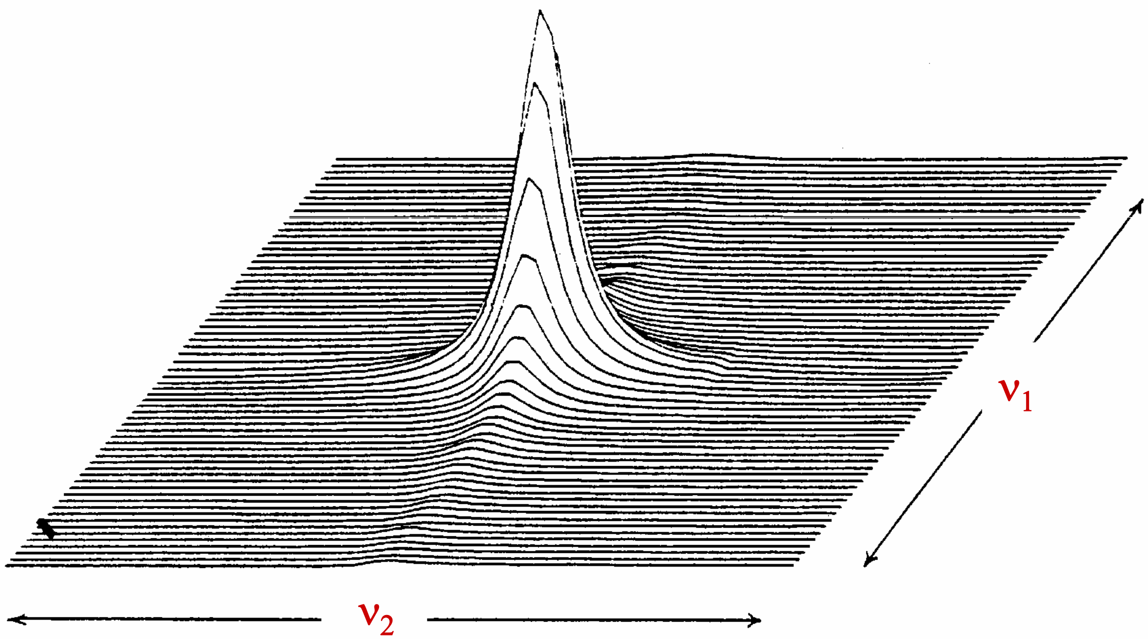




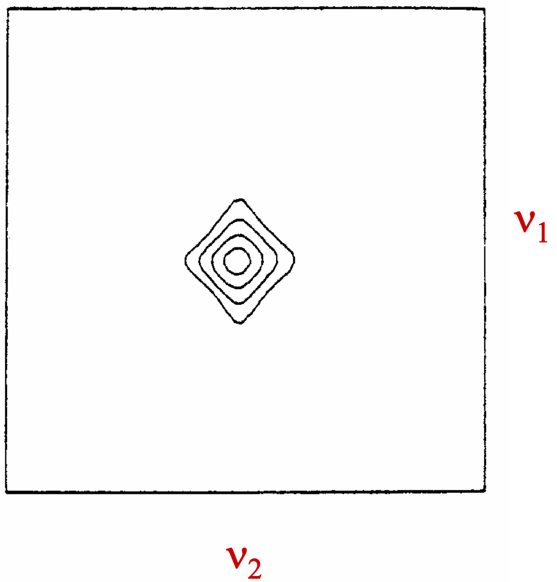
Principles of 2D NMR Spectroscopy



Principles of 2D NMR Spectroscopy

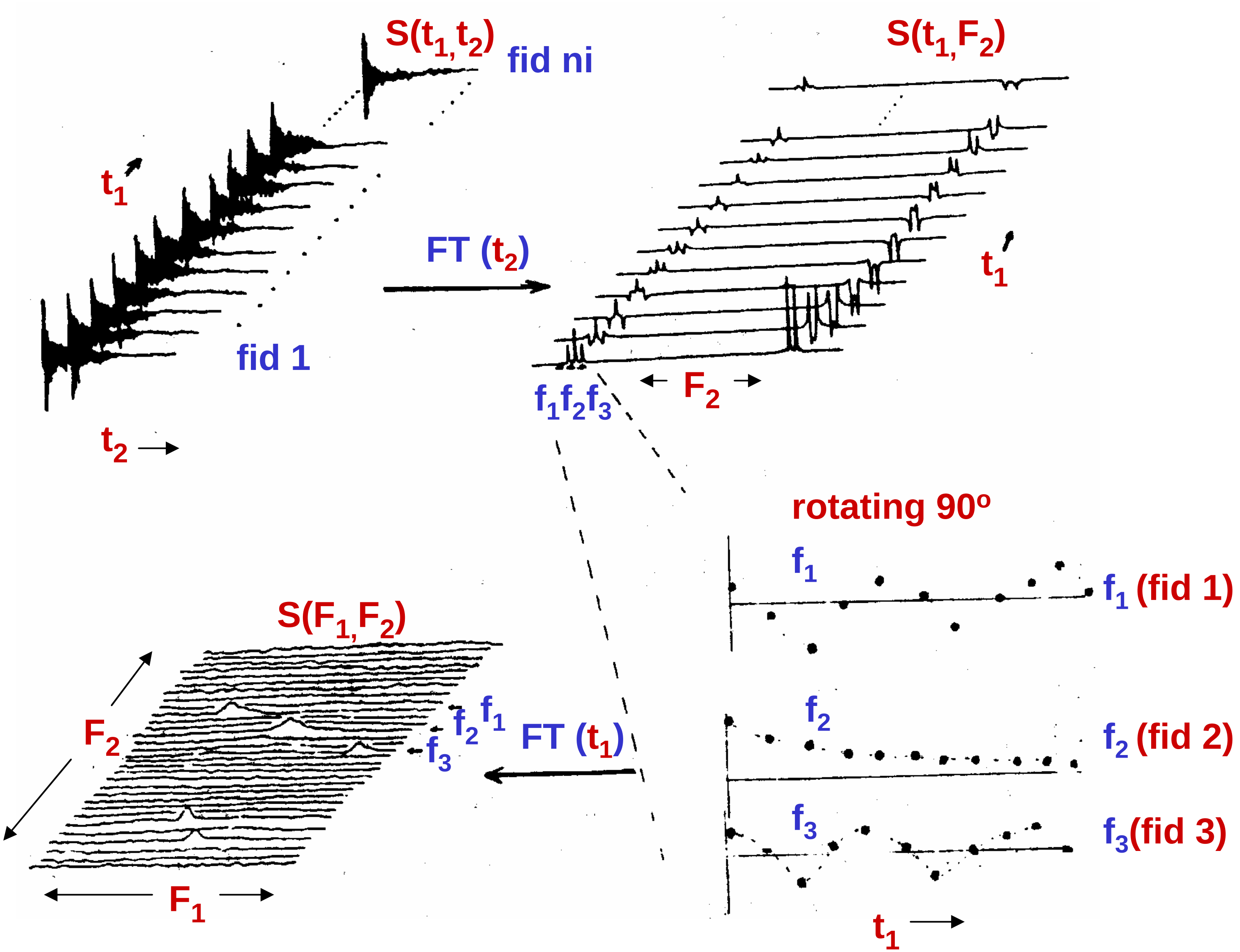


Stacked plot

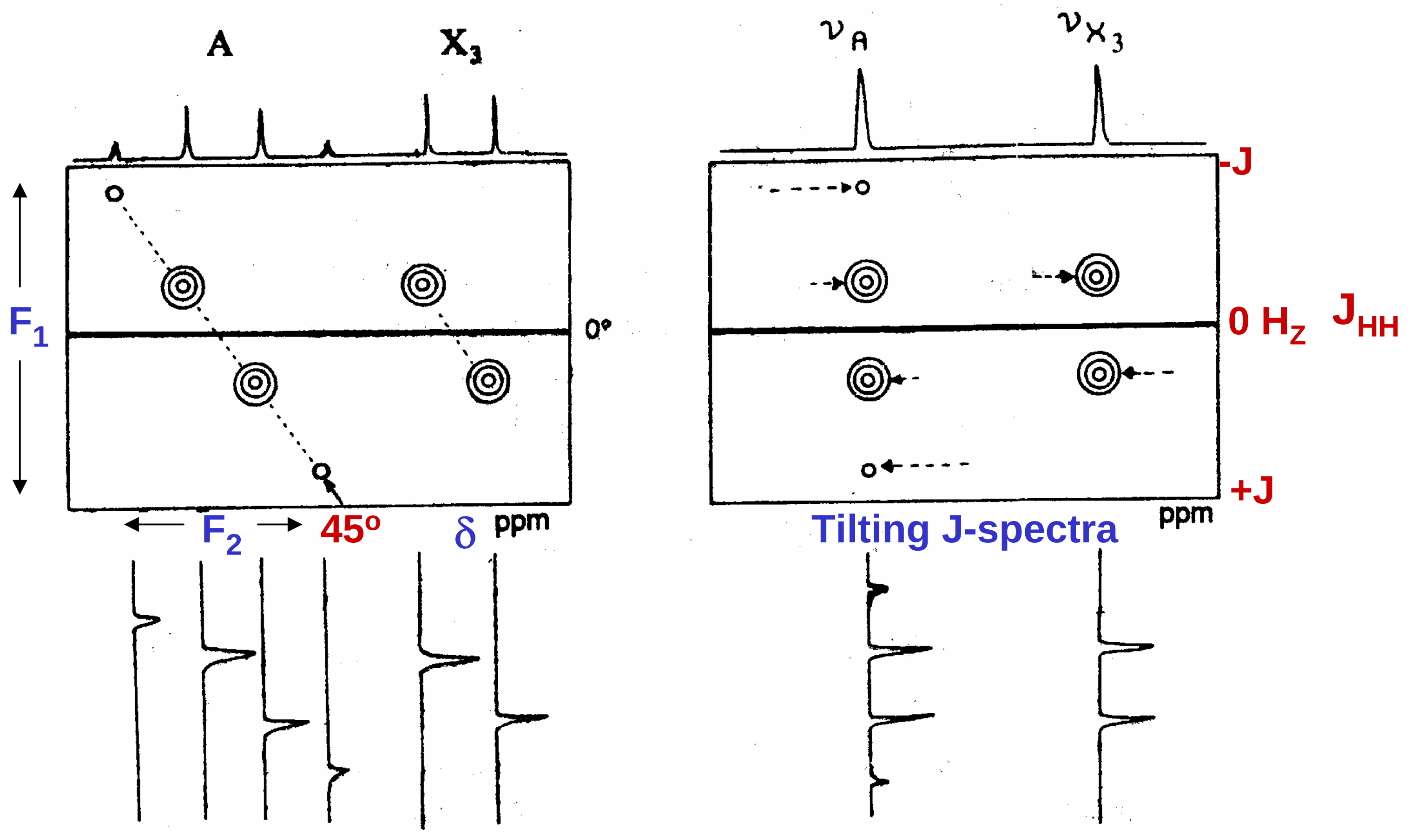


contour plot

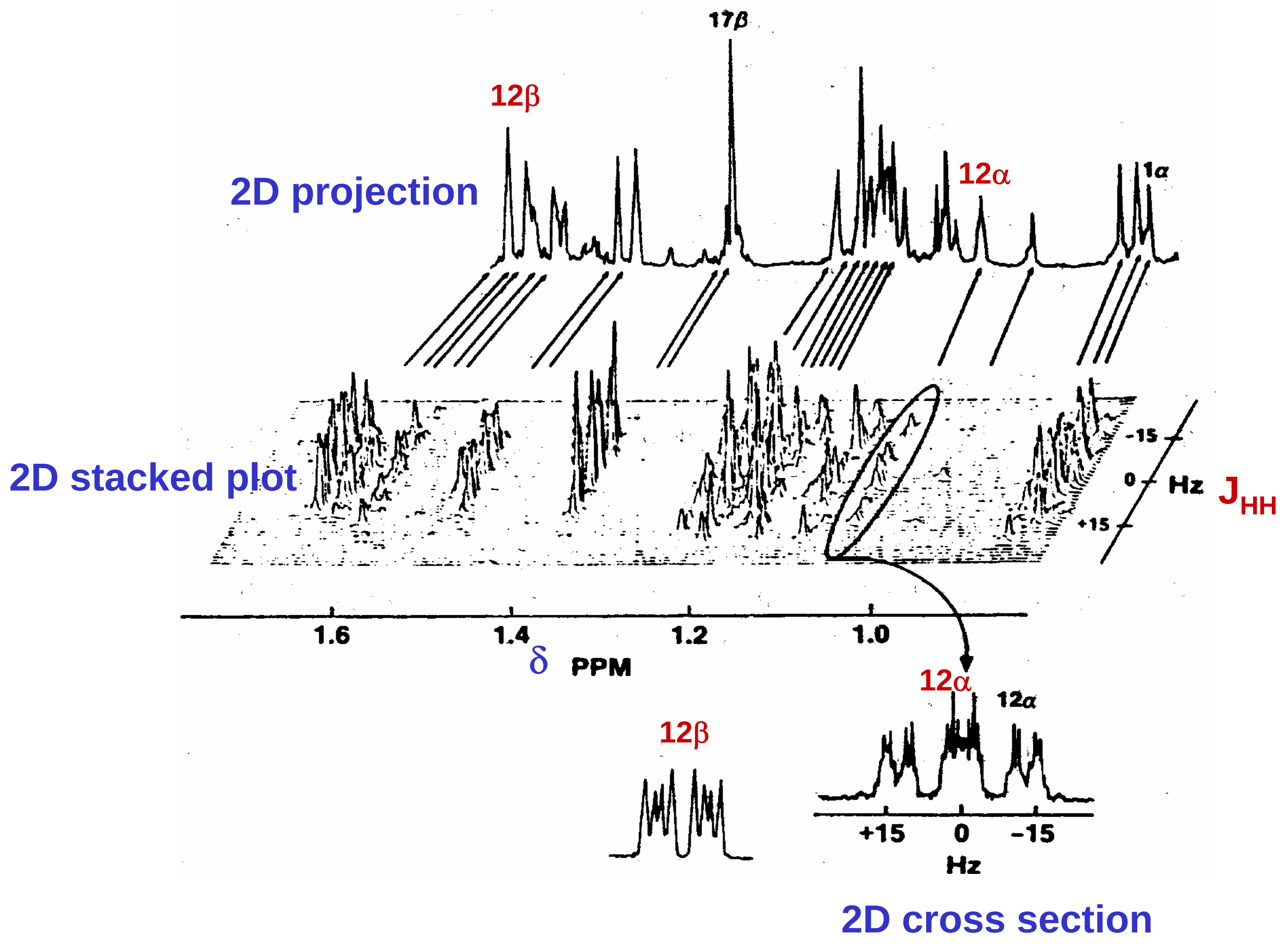
Principles of 2D NMR Spectroscopy



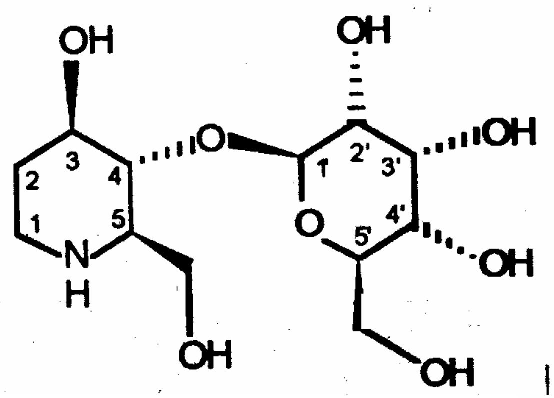
2D J-δ resolved correlation spectroscopy
The Homonuclear 2D J-Spectrum

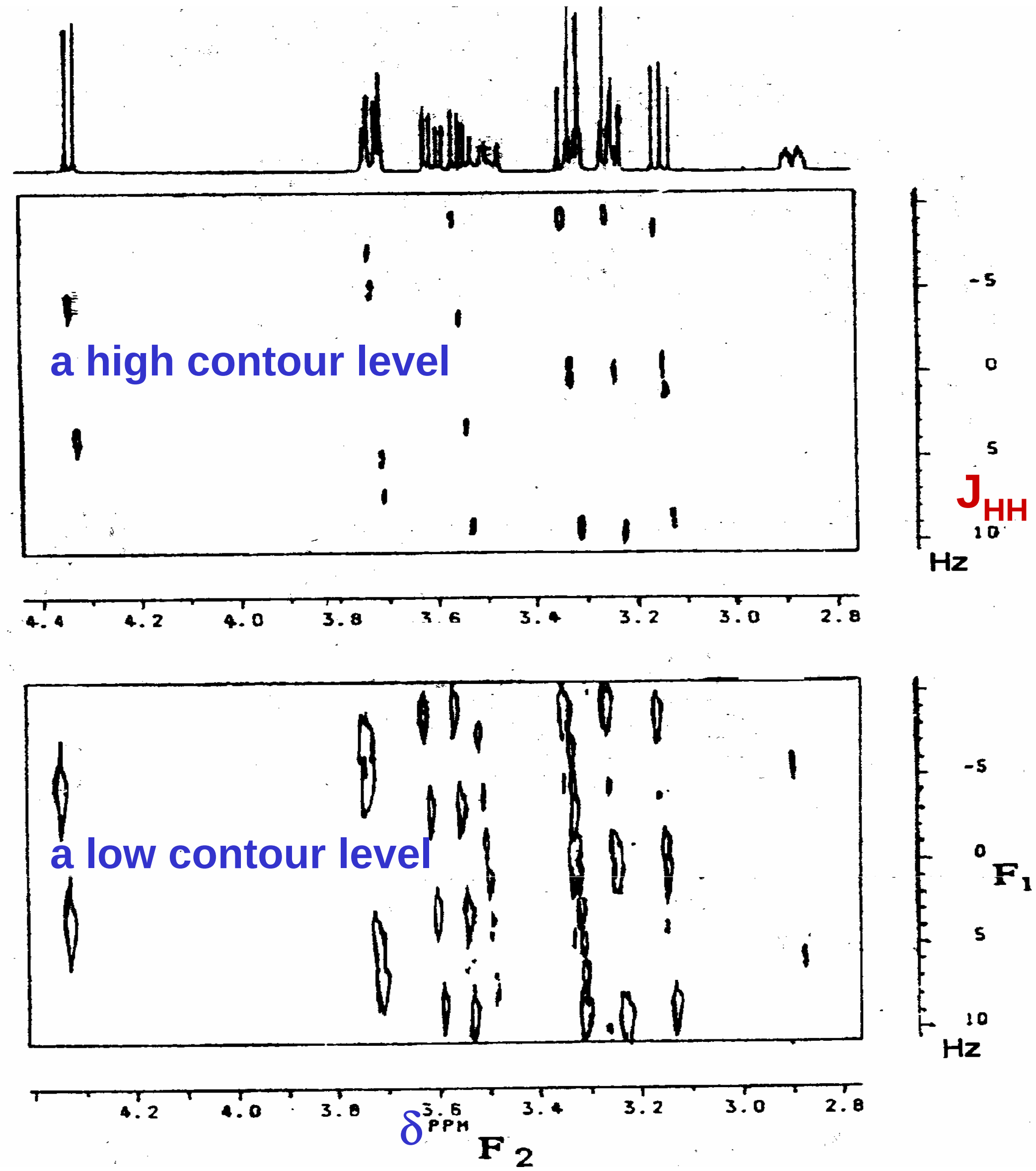


The Homonuclear 2D J-δ Spectrum

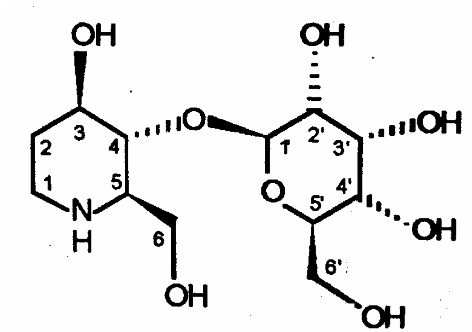


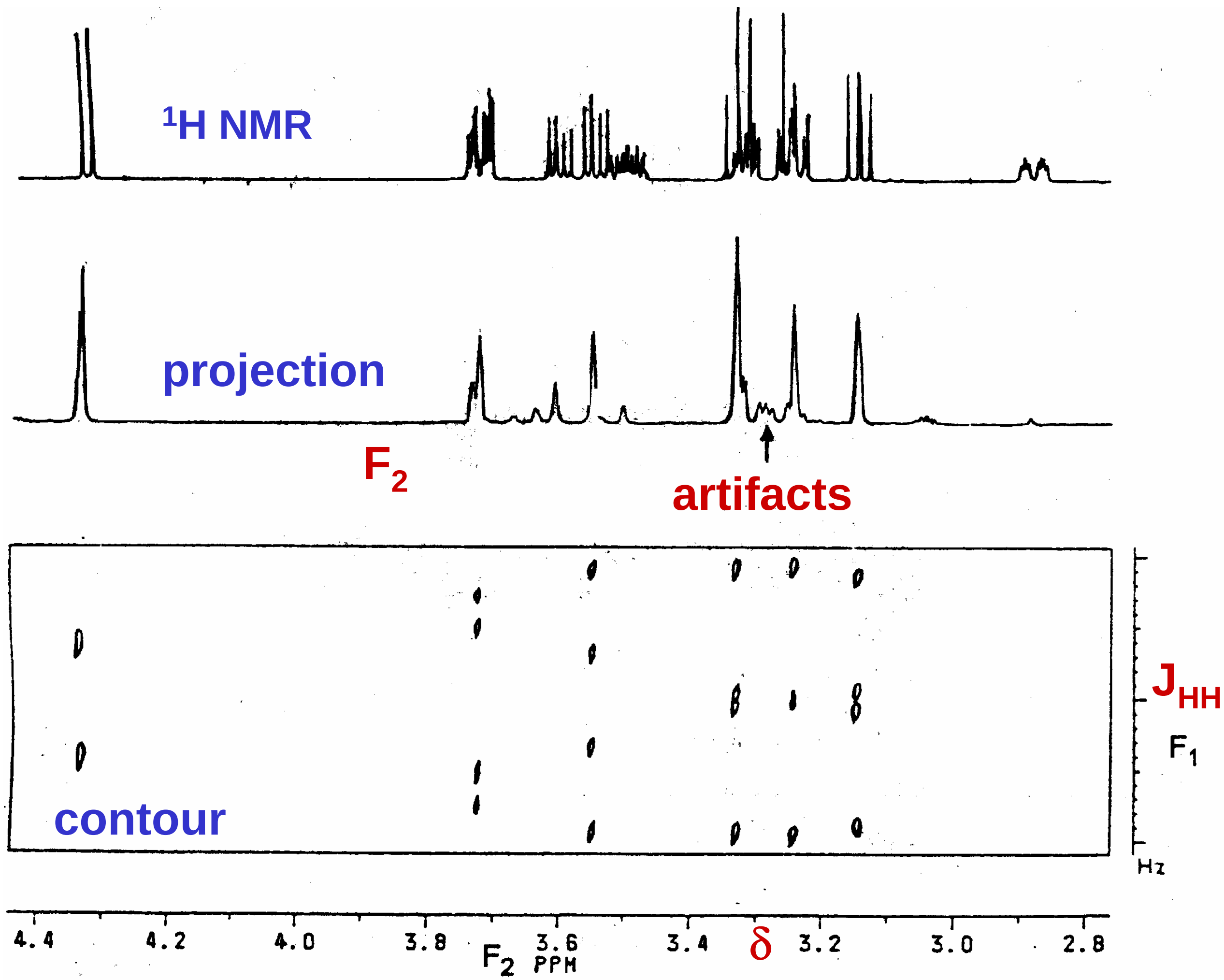
The Homonuclear 2D J-δ Spectrum



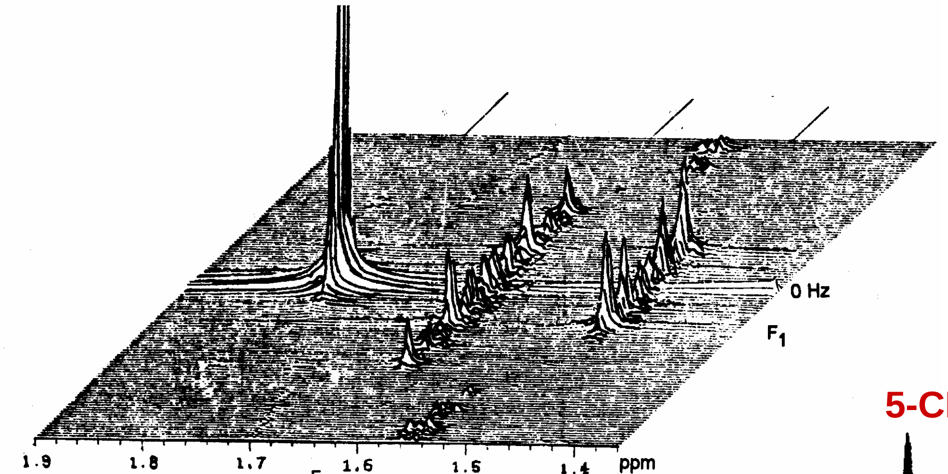


The Homonuclear 2D J-δ Spectrum

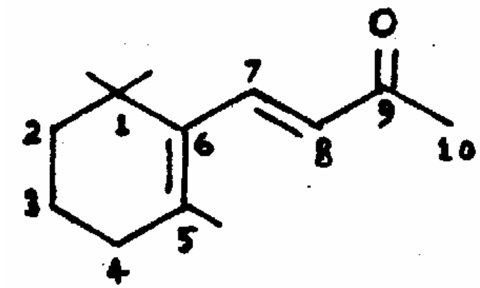




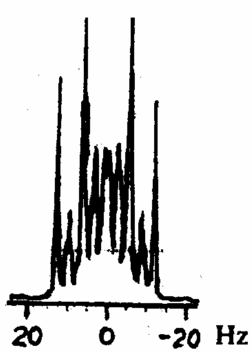
The Homonuclear 2D J-δ Spectrum of β-ionone



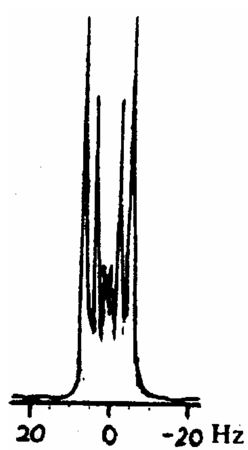
stacked plot



3-H



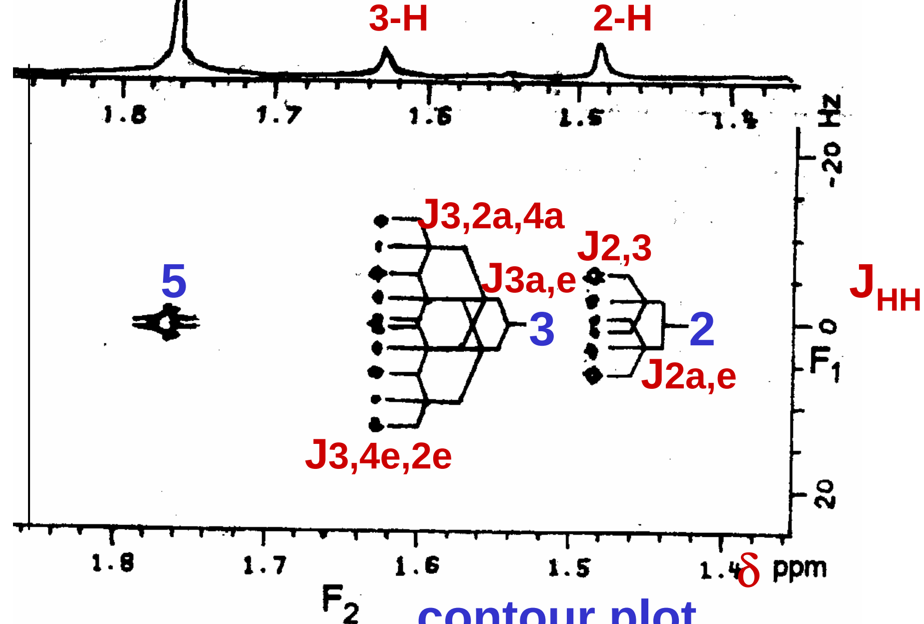
2-H



cross section

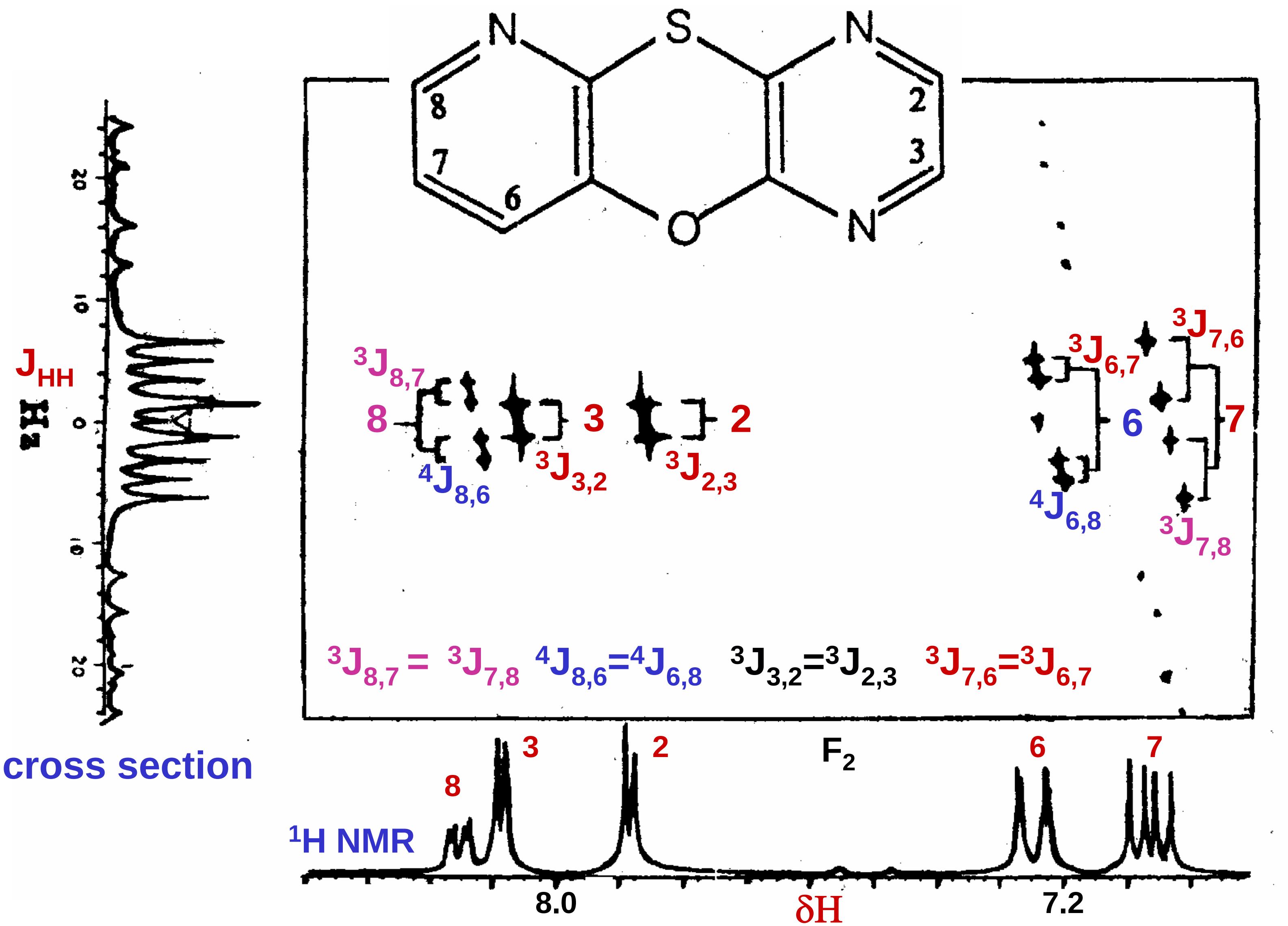
5-CH$_3$

projection

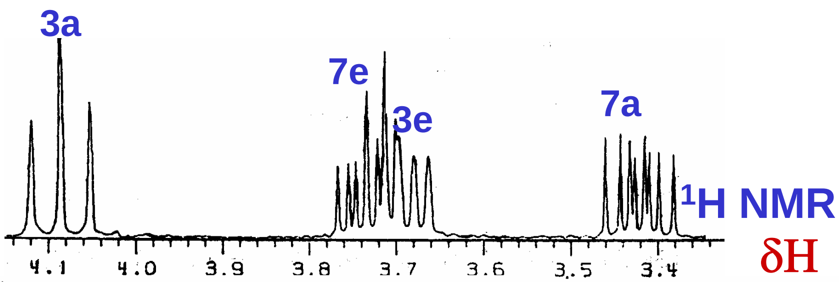


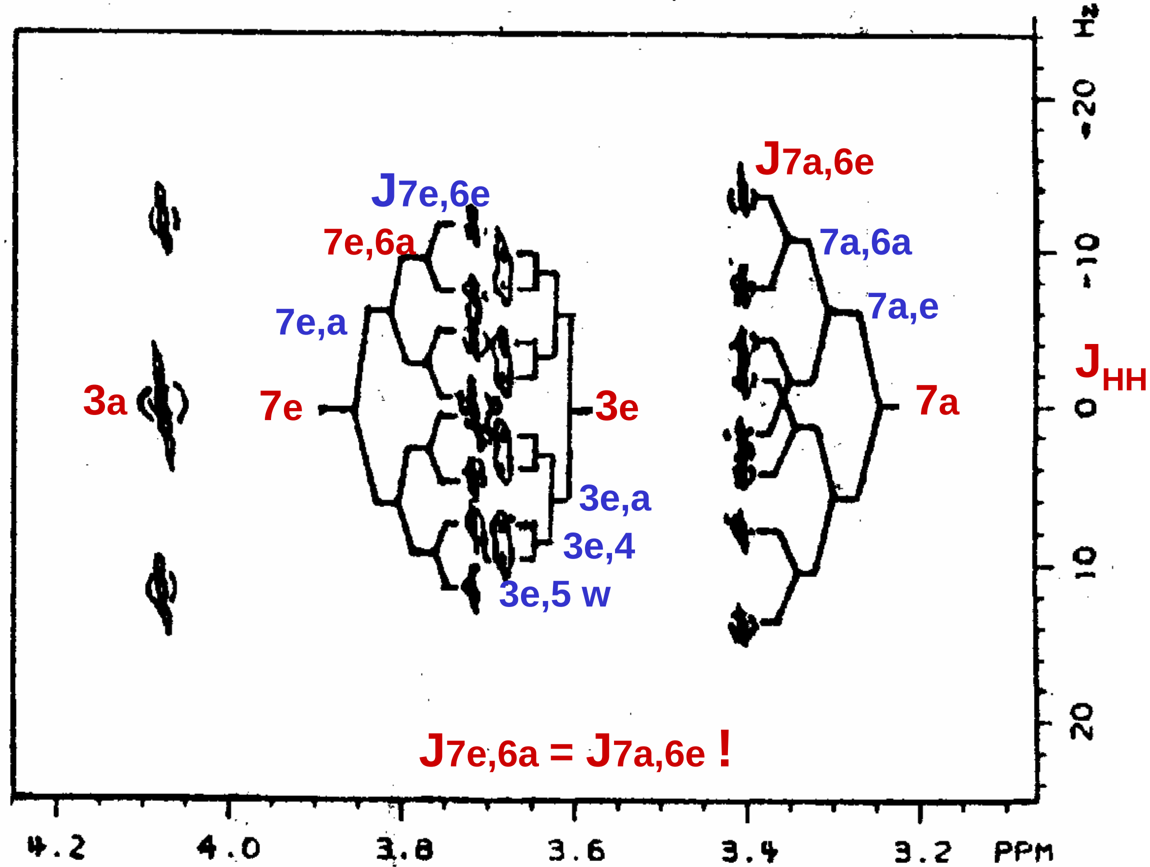
contour plot

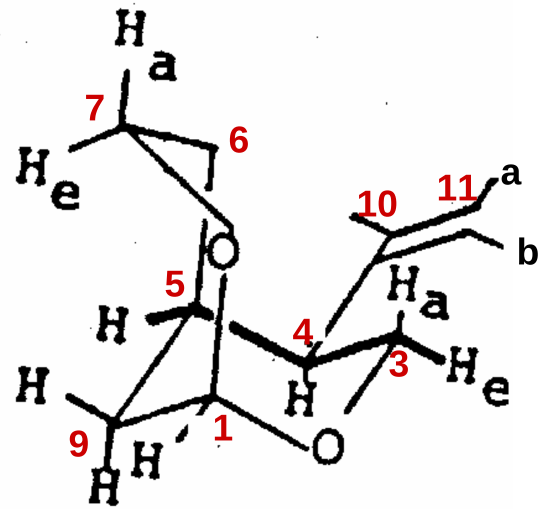
The Homonuclear 2D J-δ Spectrum of 1,4,9- triazaphenoxanthin

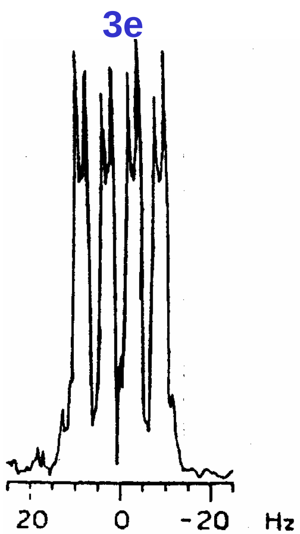


The Homonuclear 2D J-δ Spectrum of Semburin



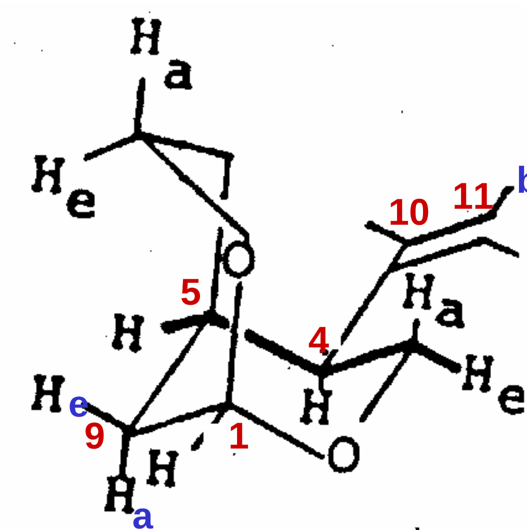


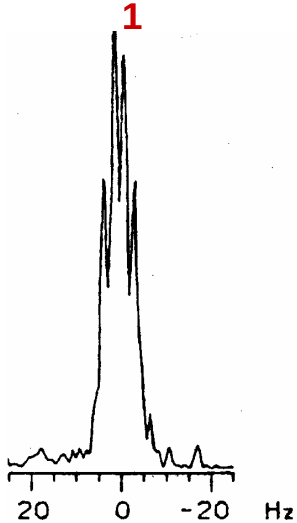


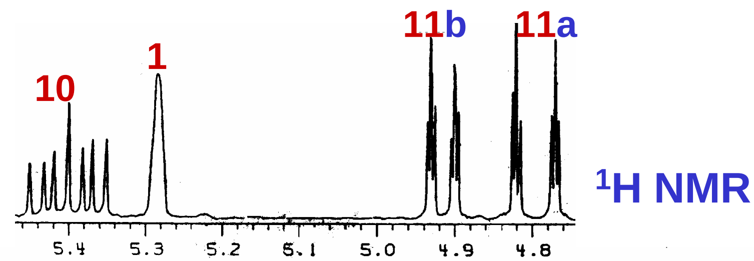


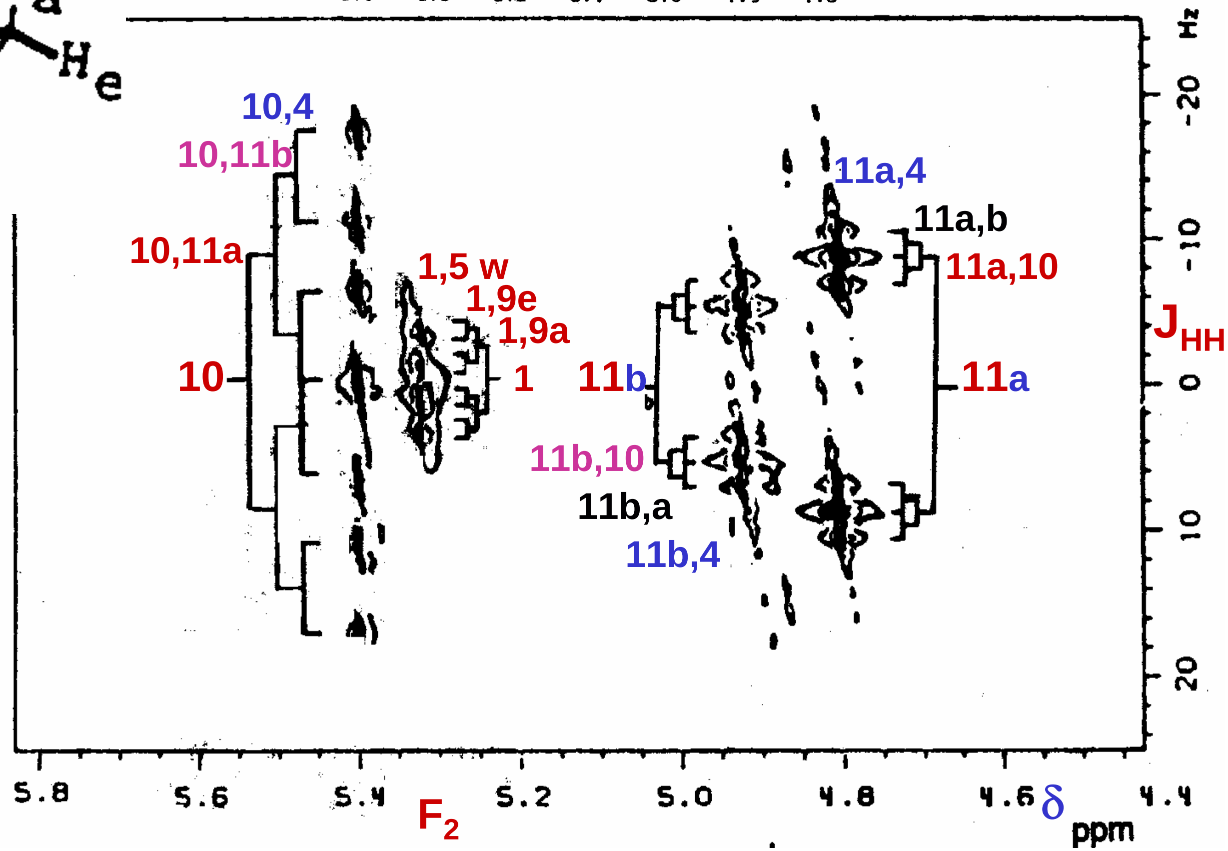
cross section

The Homonuclear 2D J-δ Spectrum of Semburin

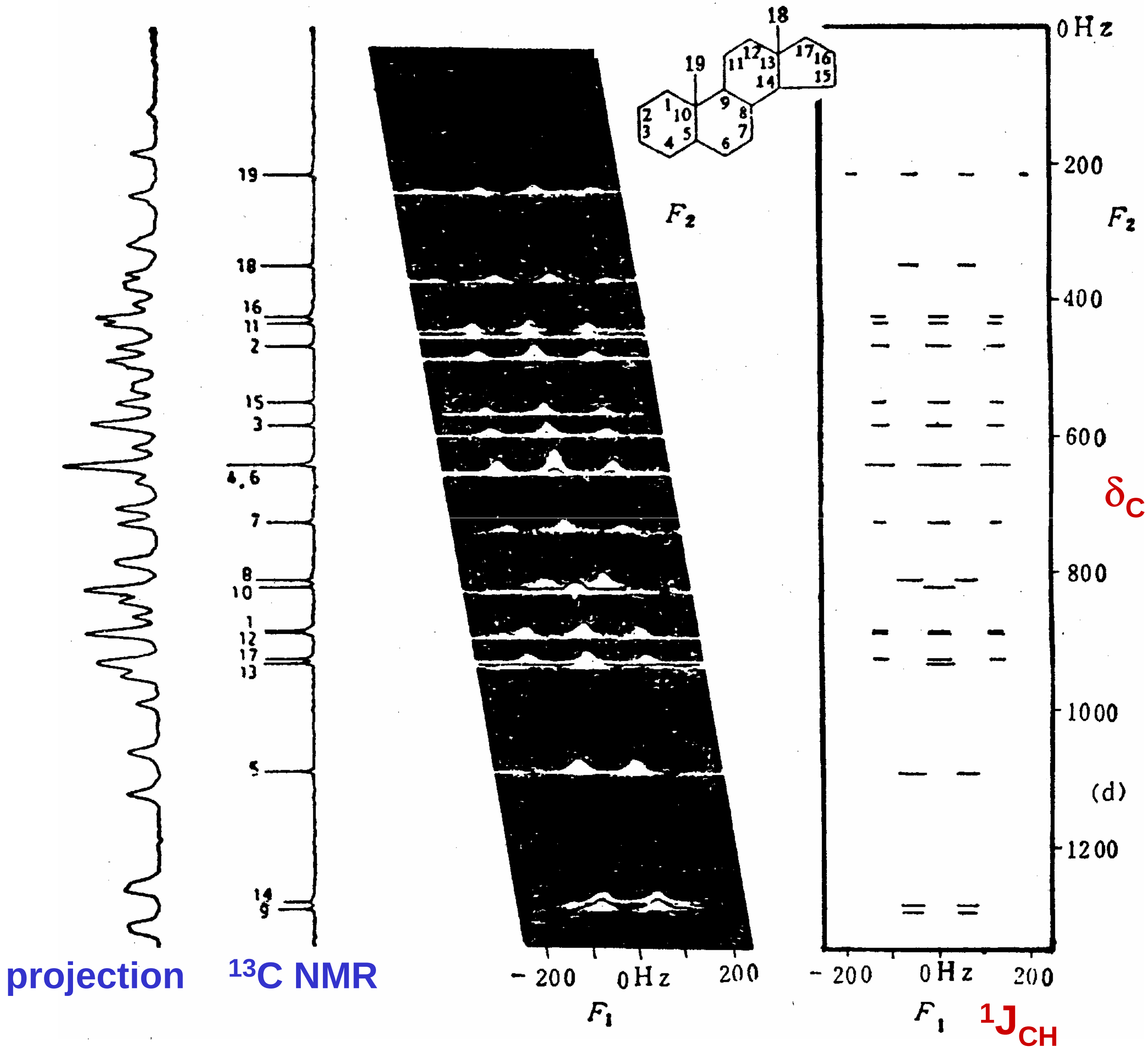




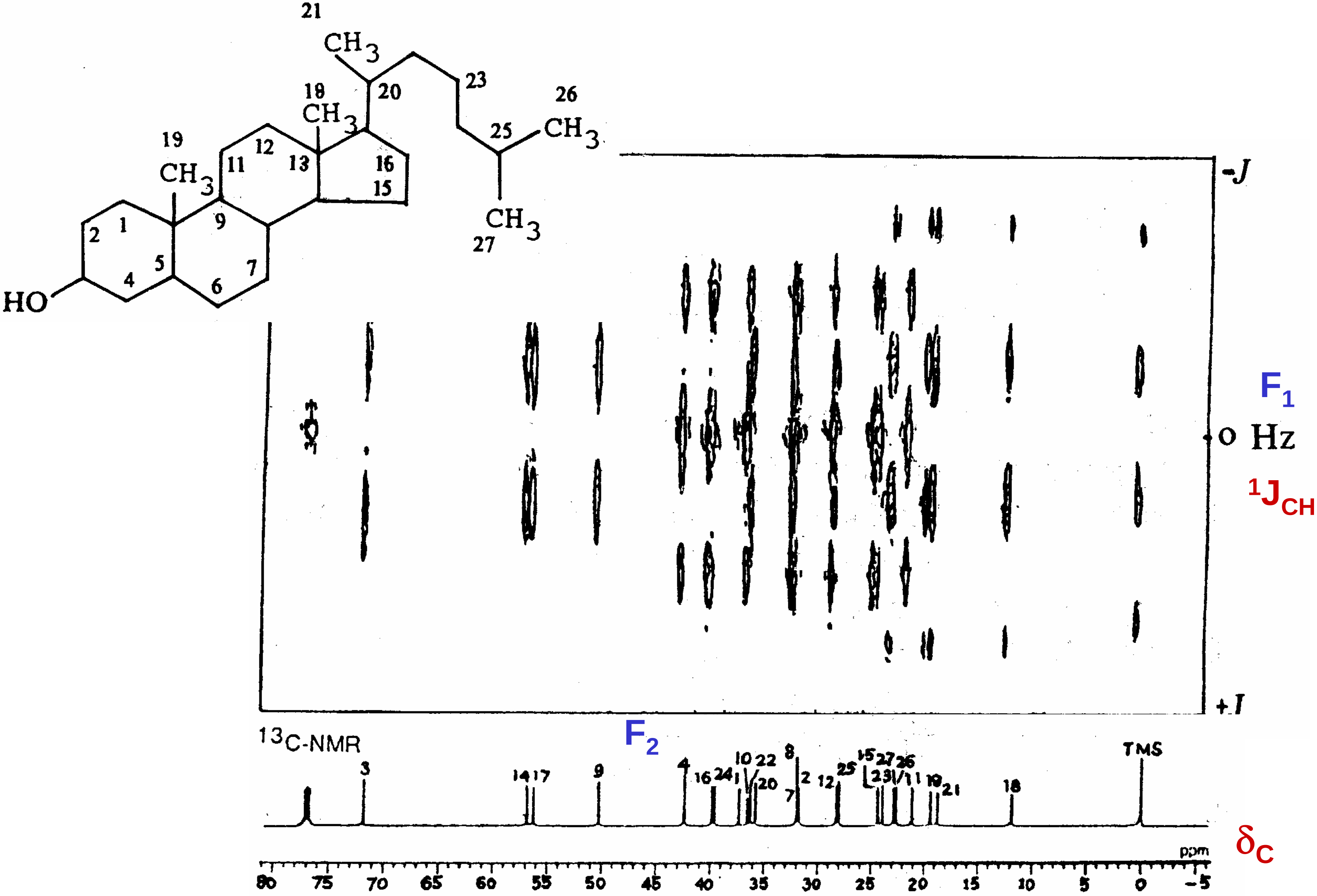




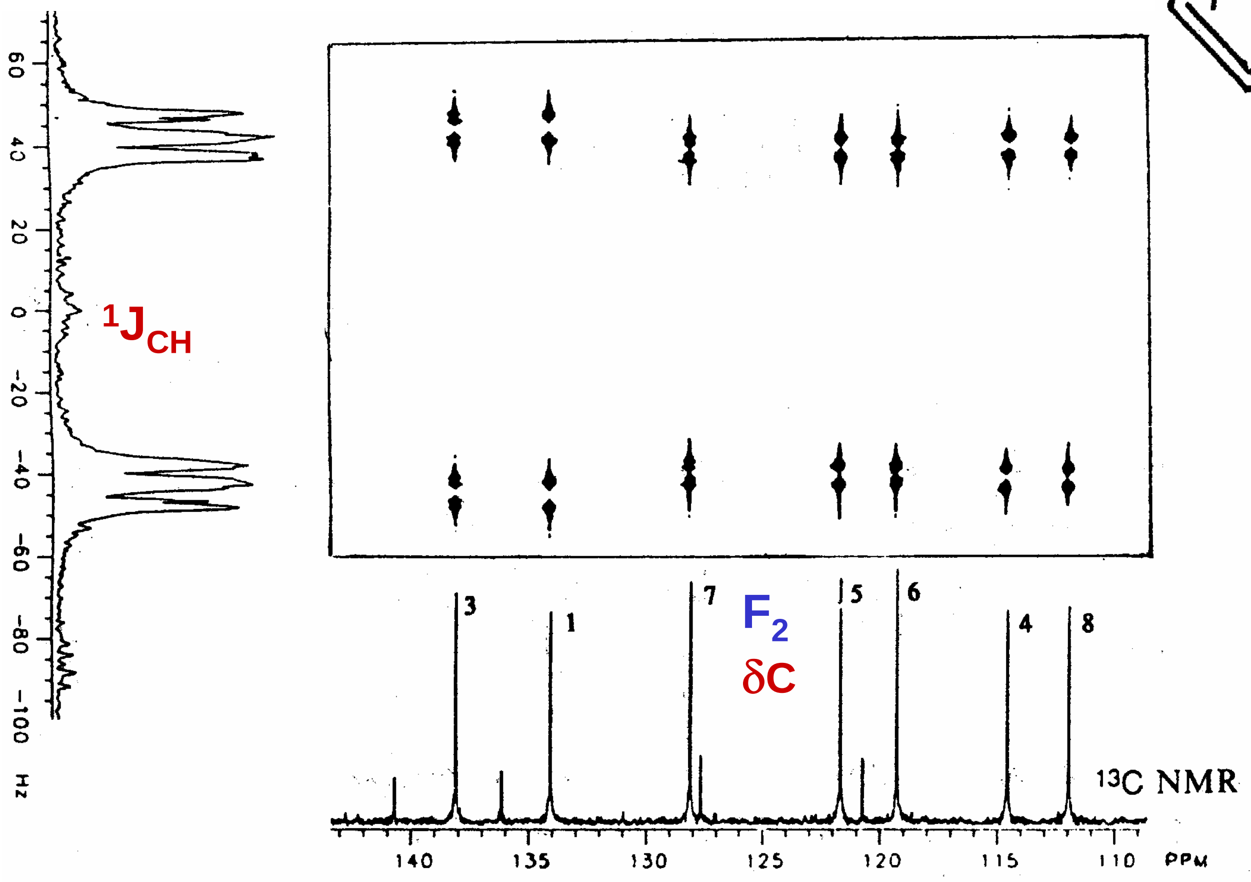
The Heteronuclear 2D C,H J-δ Spectrum of 5α–Androstane

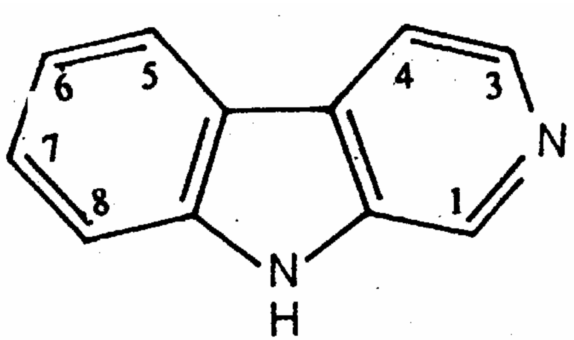


The Heteronuclear 2D C,H J-δ Spectrum of Cholestanol

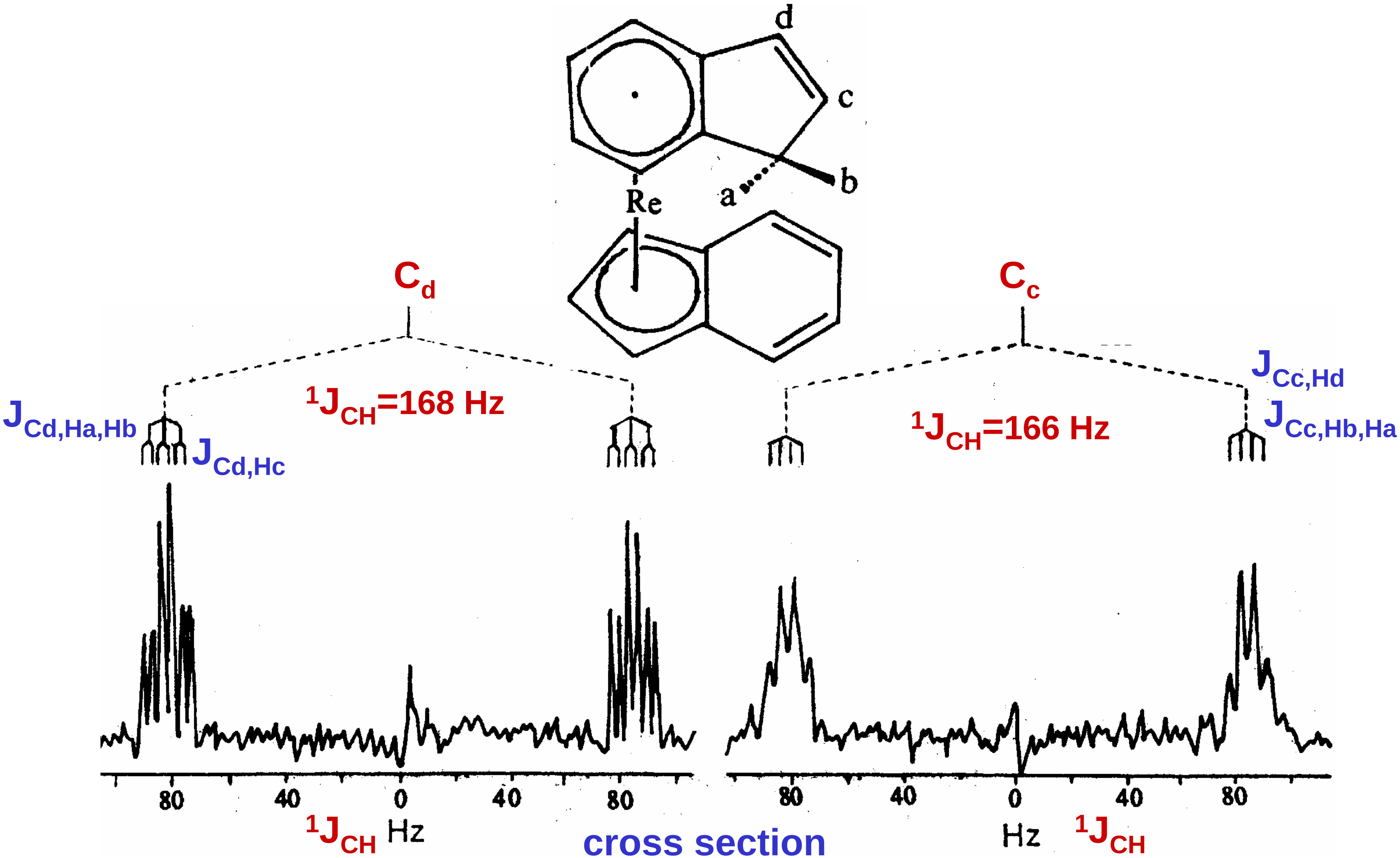


The Heteronuclear 2D J-δ Spectrum of Norharmane



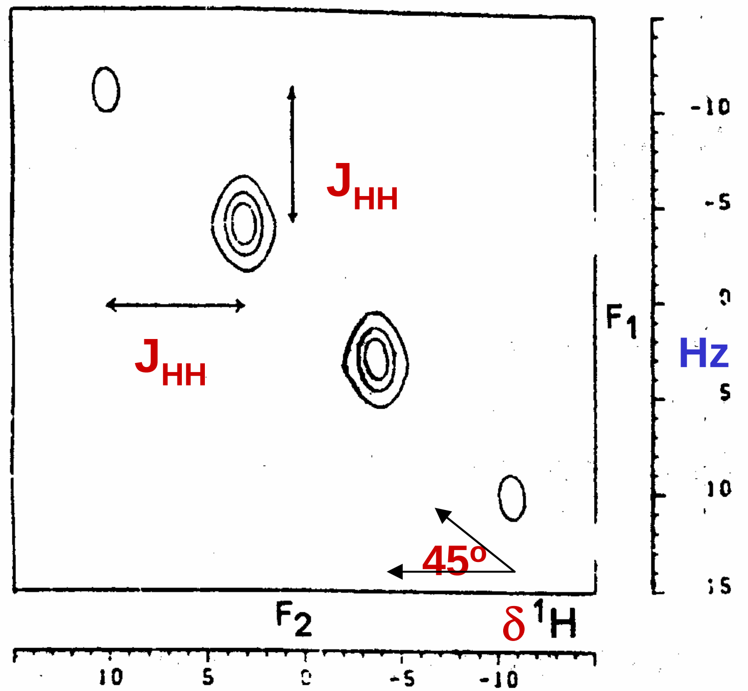


The Heteronuclear 2D C,H J-δ Spectrum

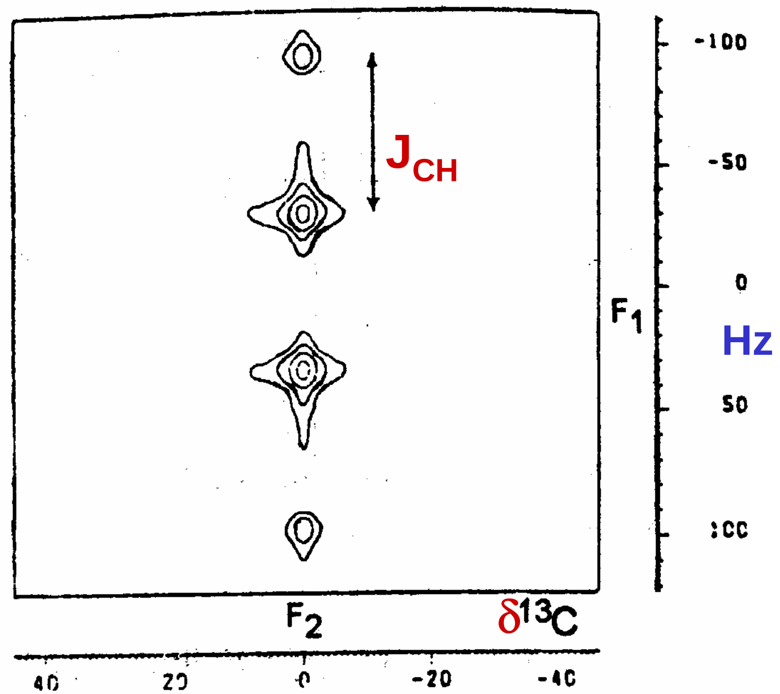


Comparision of Heteronuclear and Homonuclear 2D J-δ spectrum

Homonuclear 2D J-δSpectrum



Heteronuclear 2D J-δ Spectrum



Chapter 8
Spectral Analysis of 2D Correlation NMR Spectroscopy
Common Homonuclear 2D

2D chemical shift correlation spectroscopy:

1. **2D ^{1}H-^{1}H COSY**
   (COrrelation SpectroscopY)

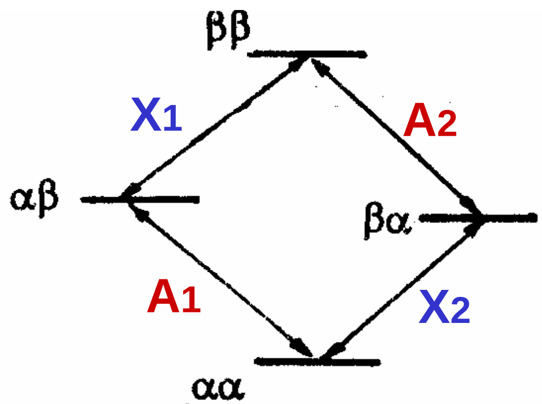
2. **^{13}C-^{13}C 2D Correlations:**
   2D- INADEQUATE
   (Incredible Natural Abundance DoublE QUantum Transfer Experiment)

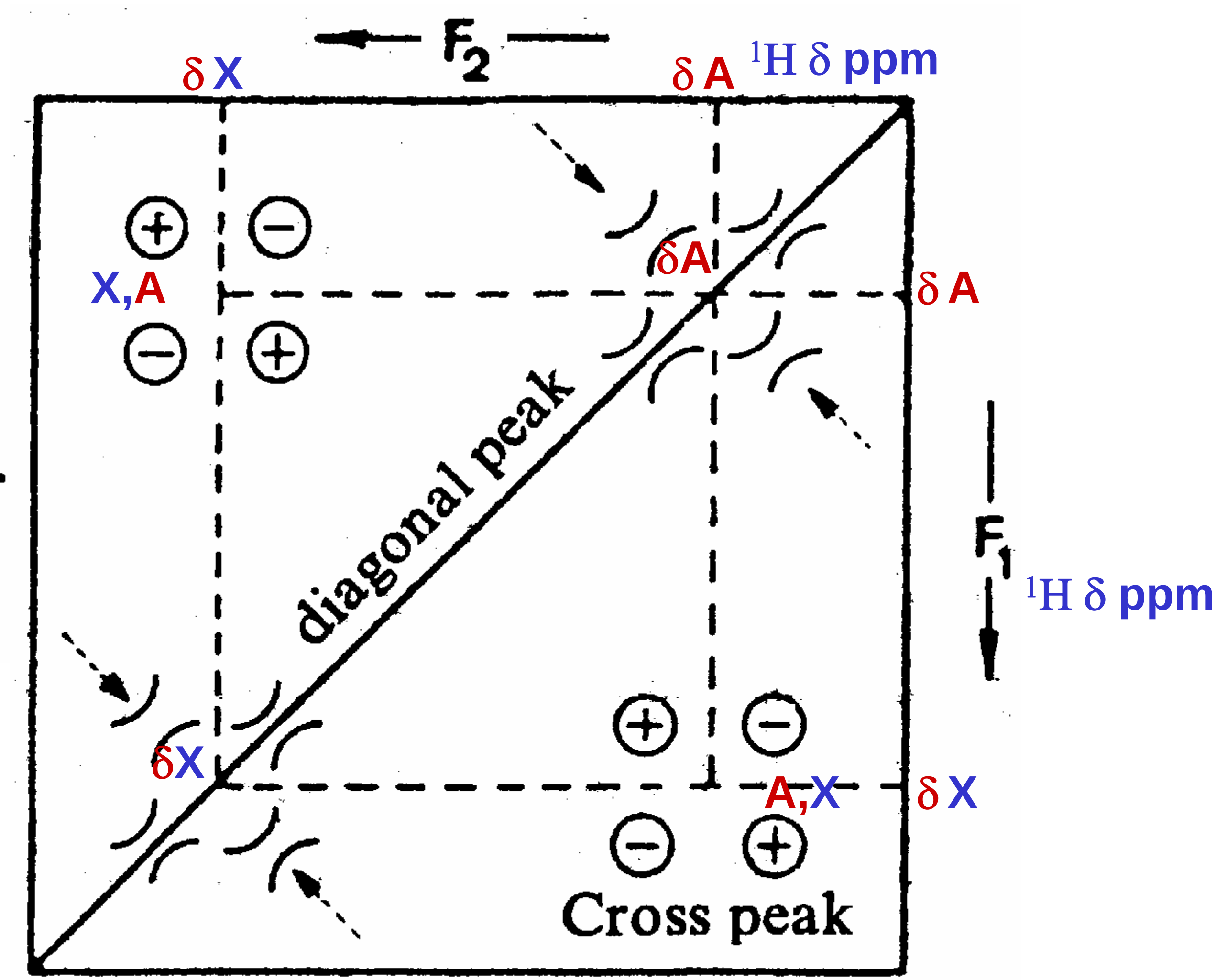
2D ^1H-^1H COSY

(COrrelation SpectroscopY)

2D chemical correlation spectroscopy)

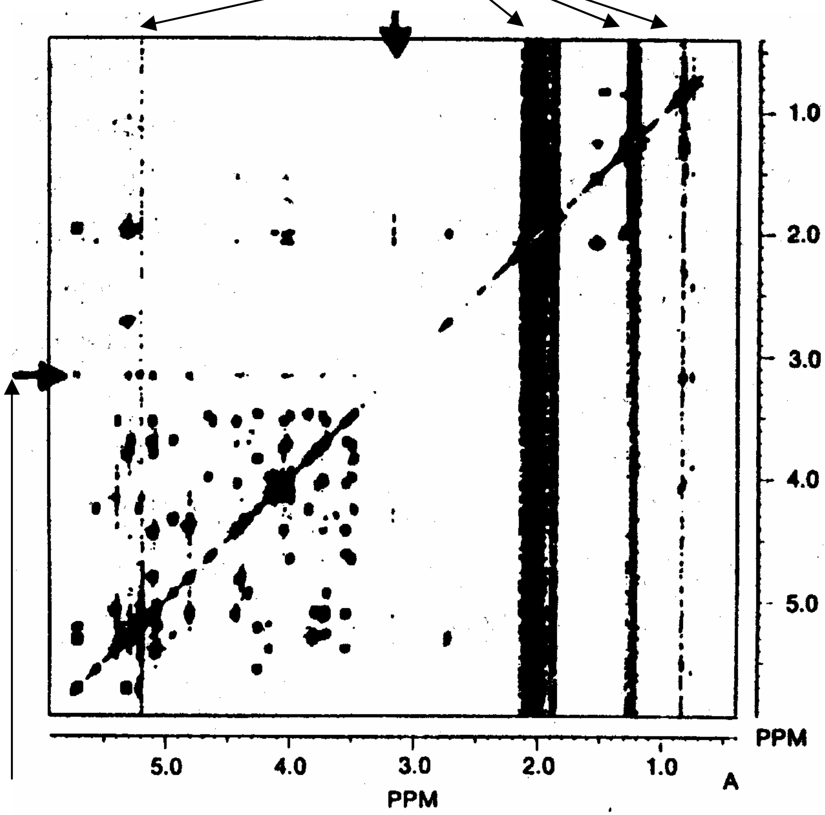
AX spin system:





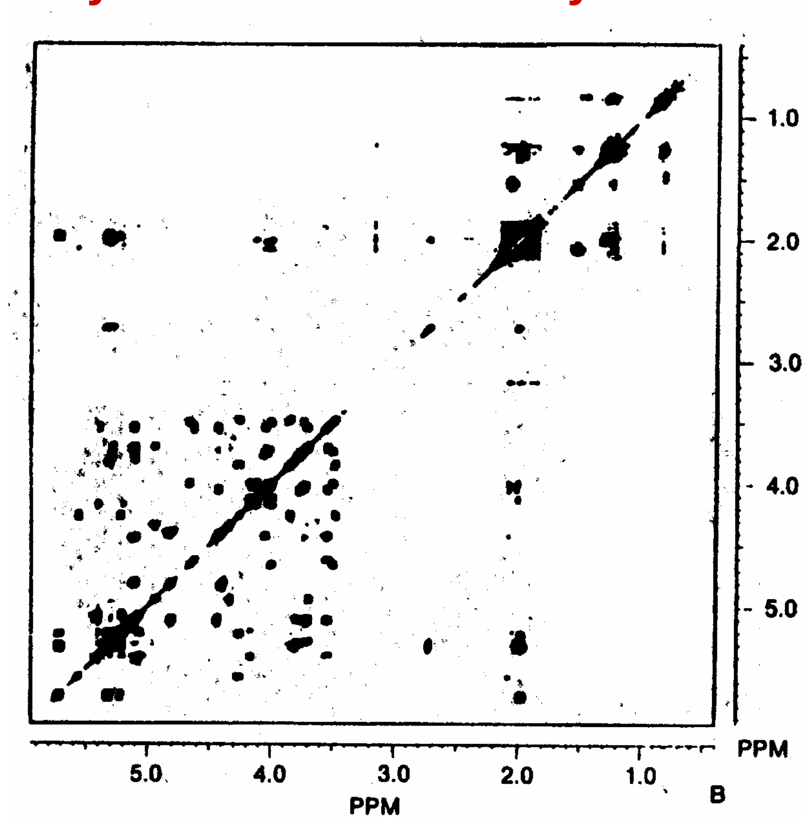
2D ^{1}H-^{1}H COSY experiment

strong F_1 noise of CH_3

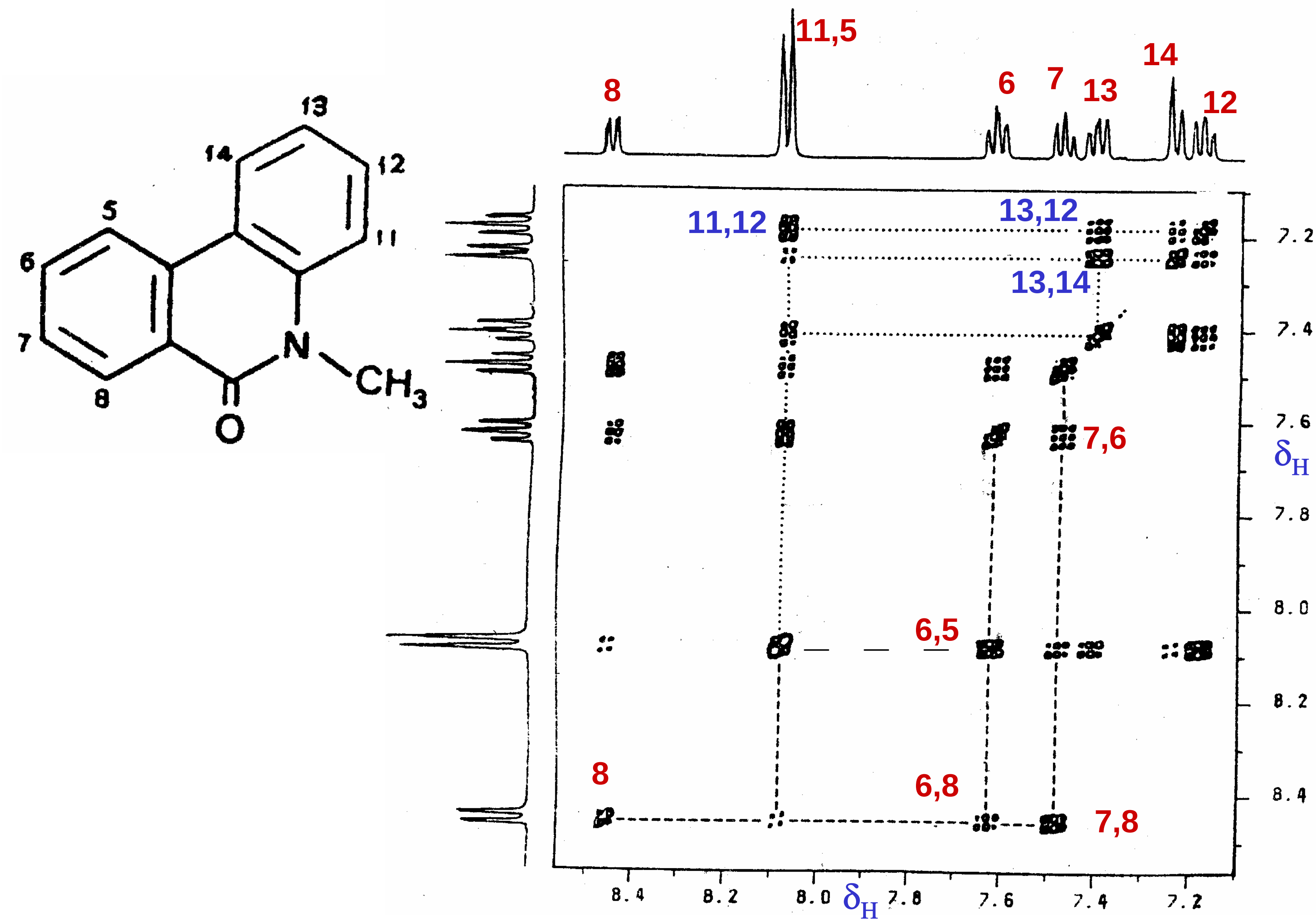


Horizontal F_1 = 0 axial peaks

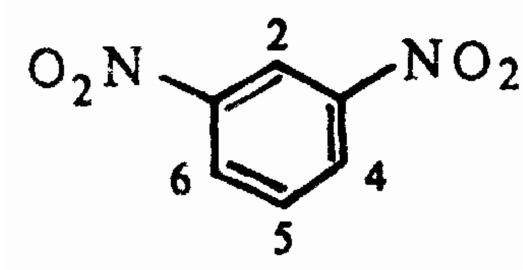
symmetrization of cosy data

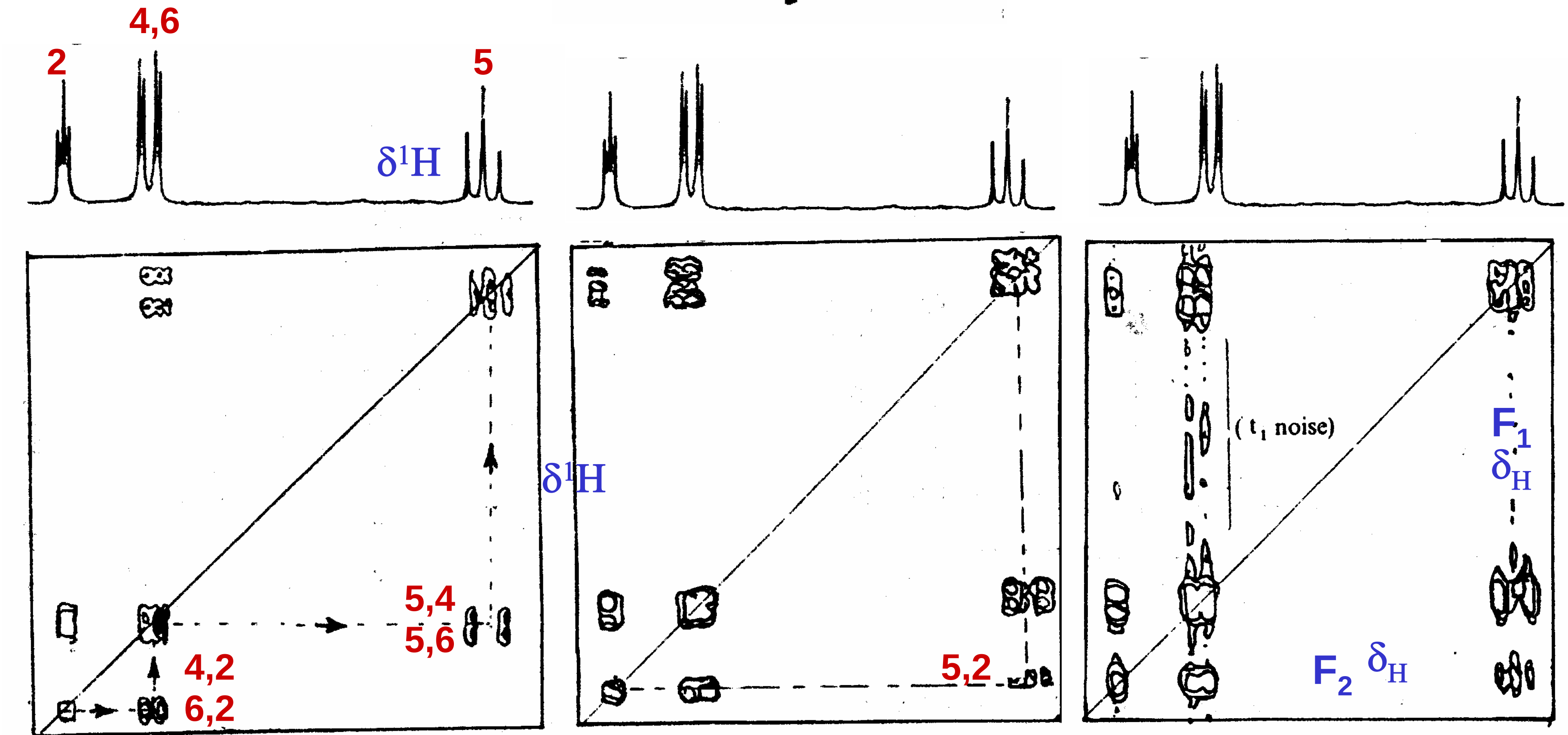


2D ^1H-^1H COSY 90º spectrum of N-methyl-benzosicarbostyril



2D ^1H-^1H COSY 90° experiment

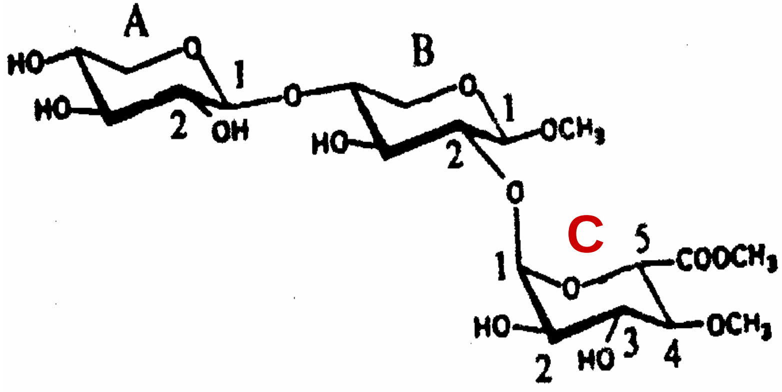


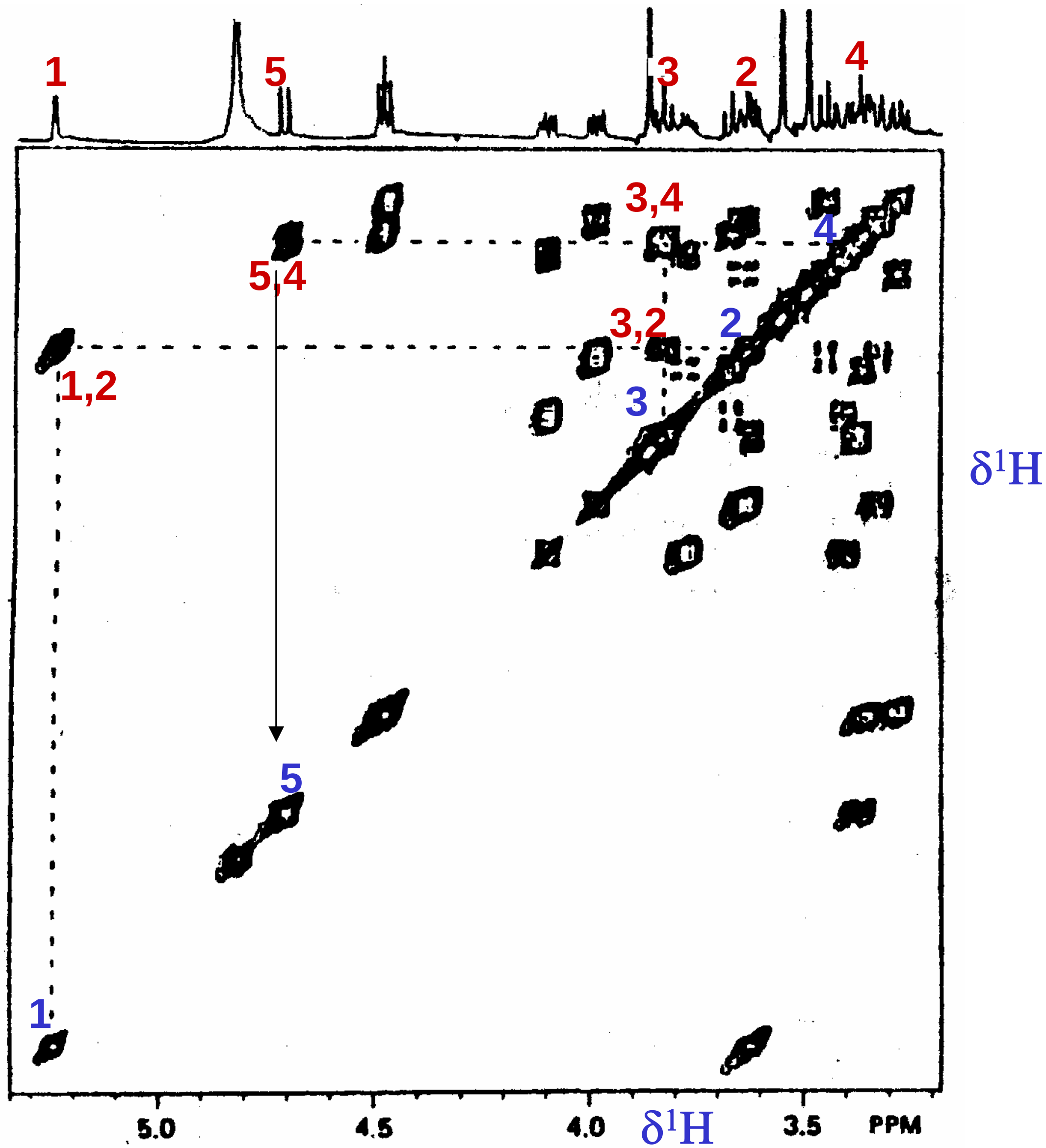


symmetrization

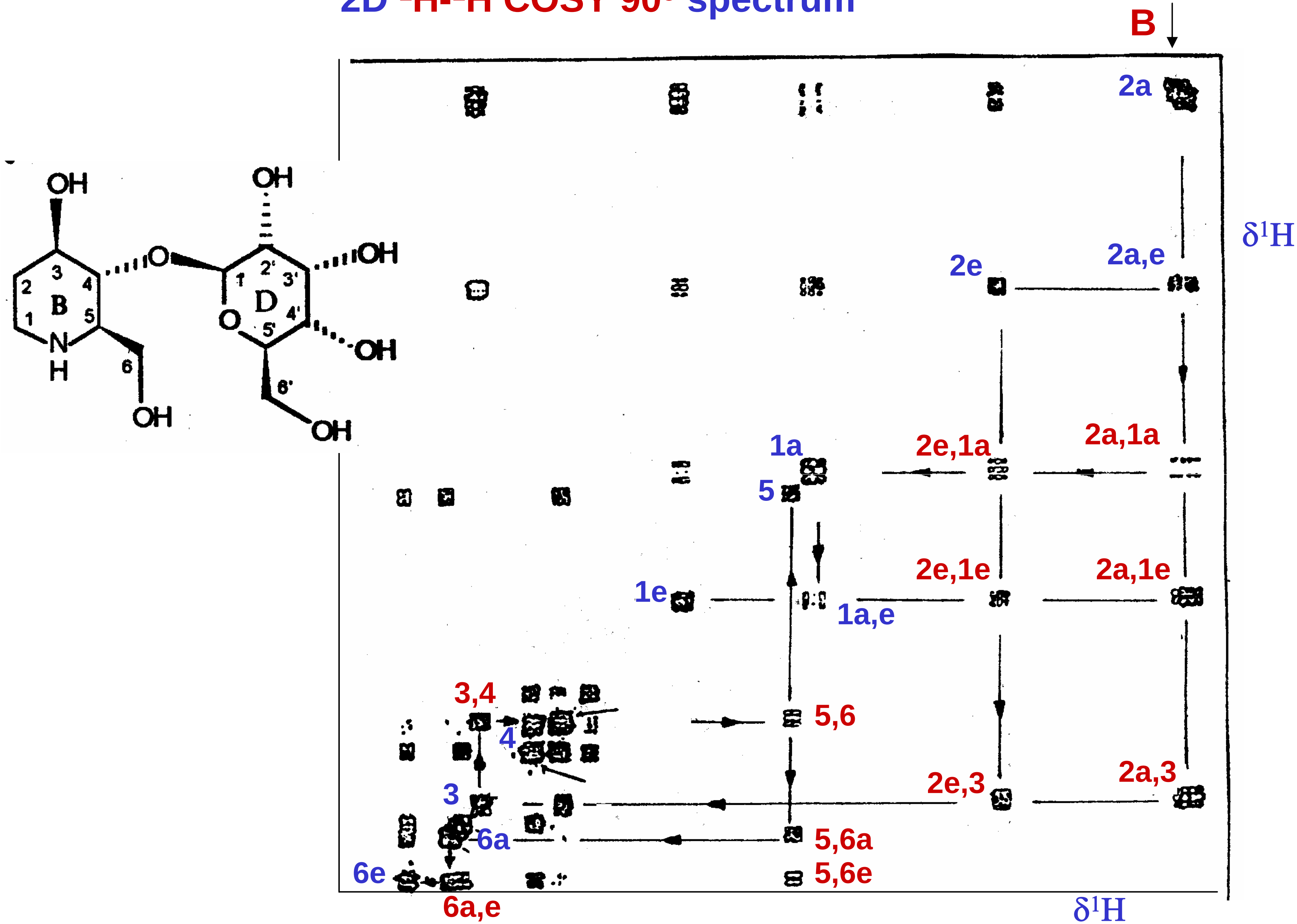
t_1- noise

2D ^1H-^1H COSY 90° spectrum

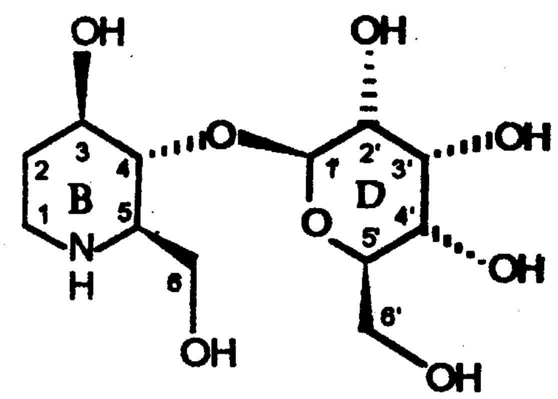


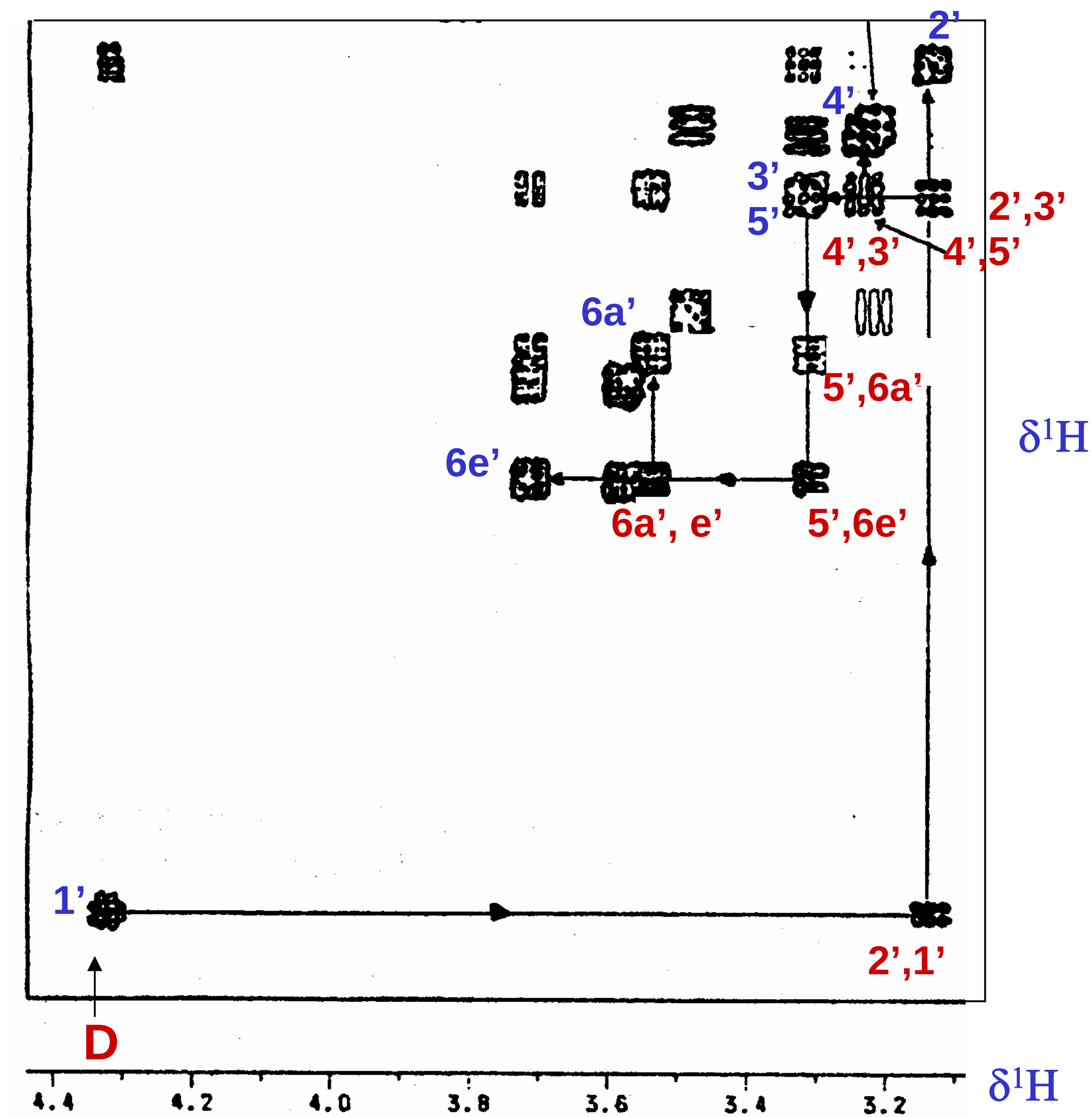


2D ^{1}H-^{1}H COSY 90° spectrum

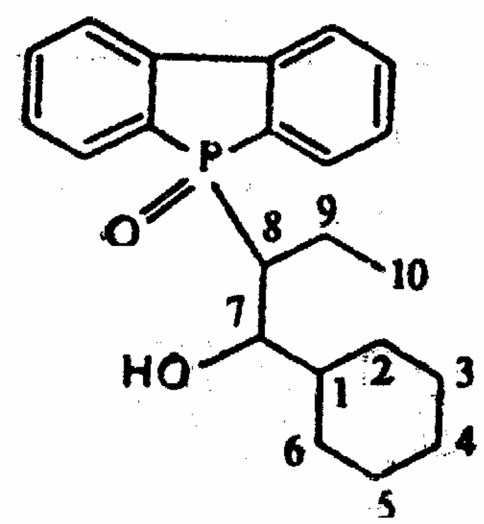


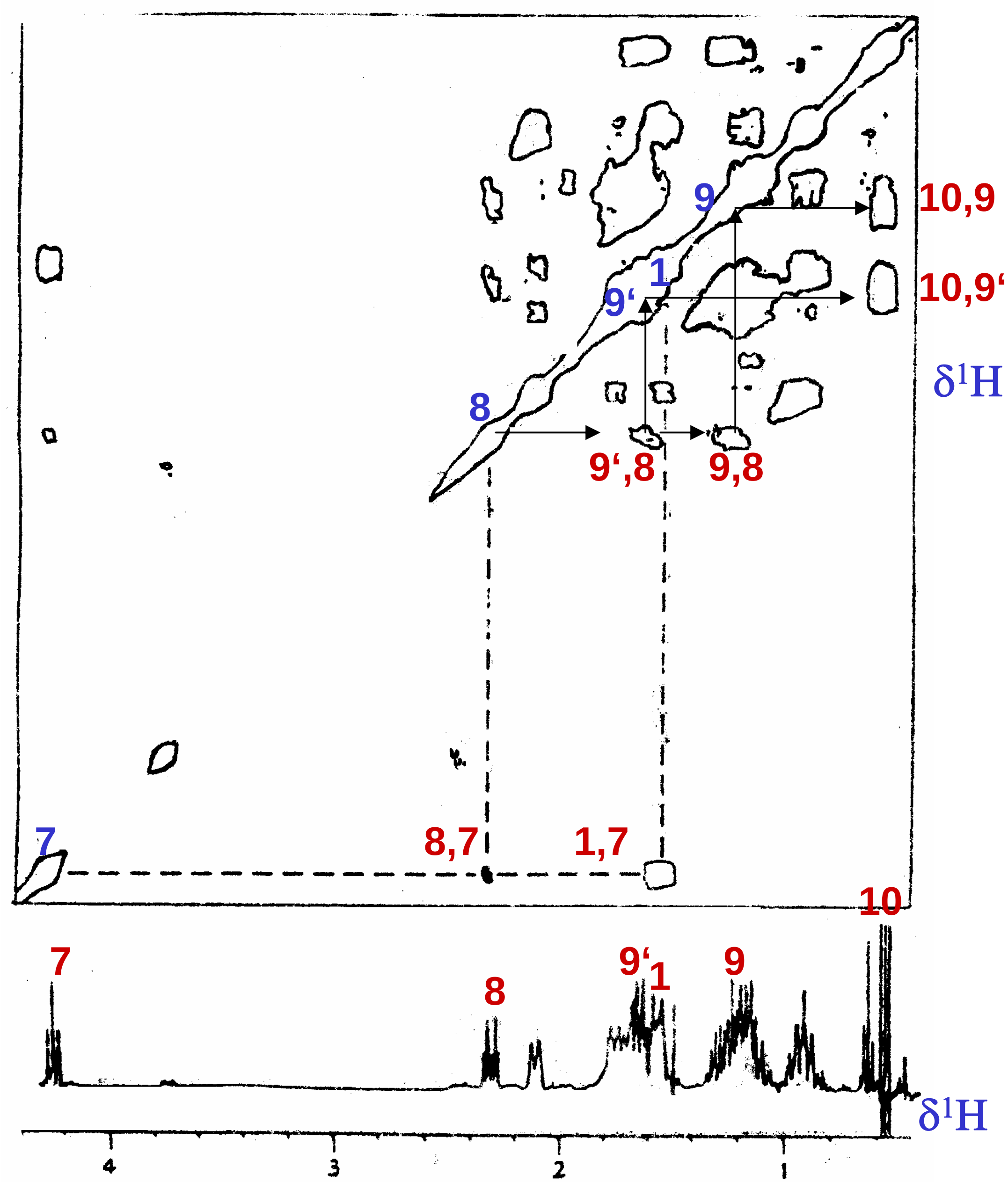
2D ^{1}H-^{1}H COSY 90° spectrum



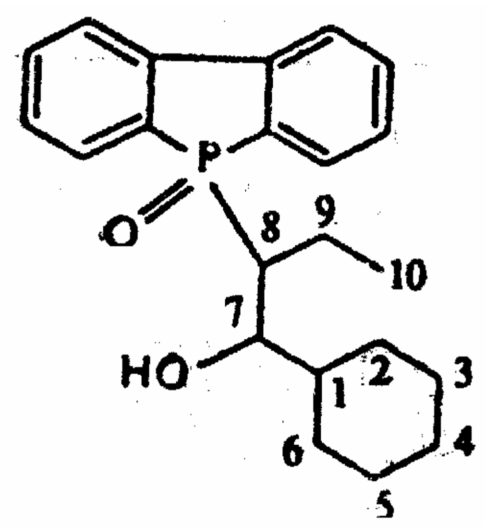


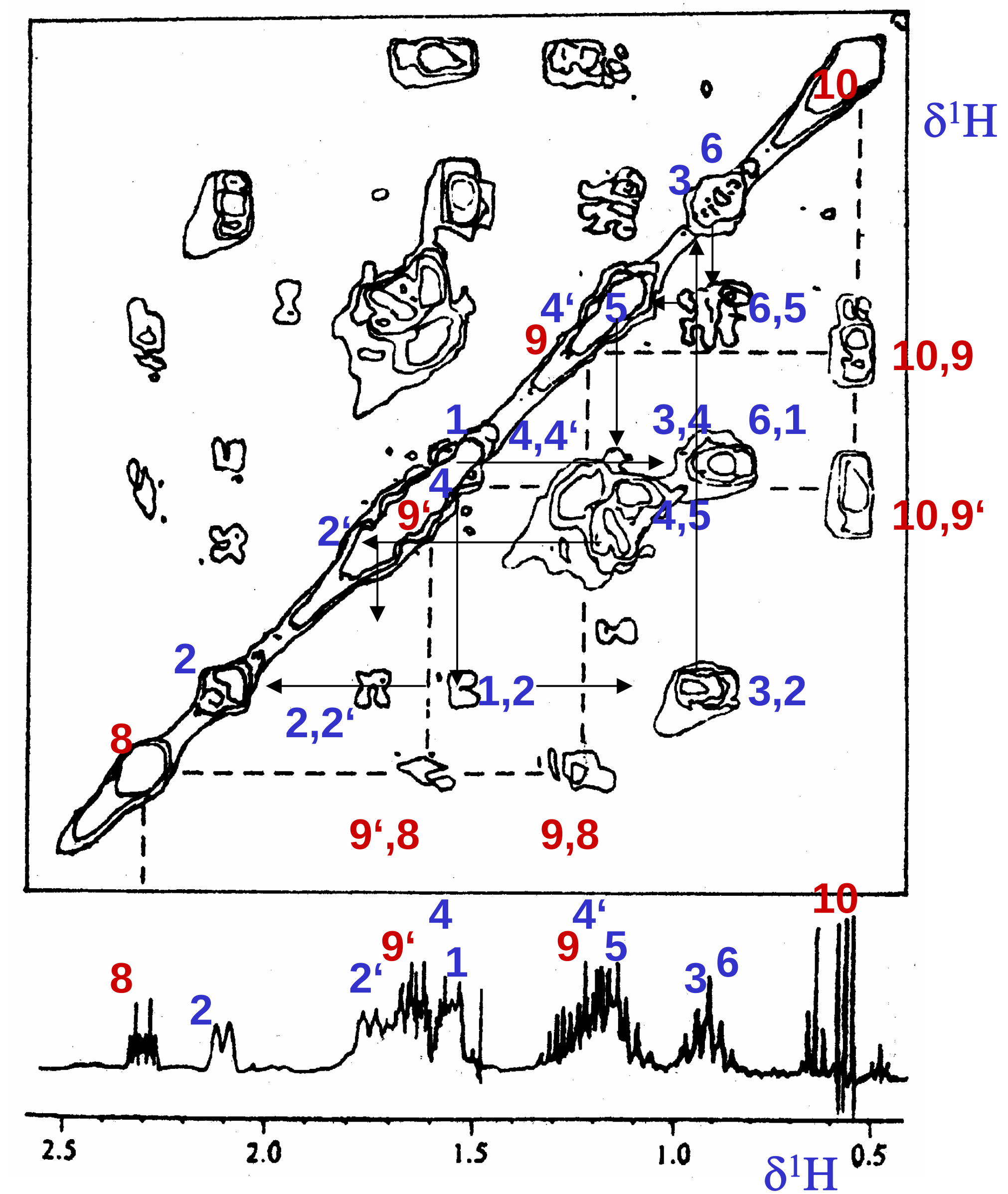
2D ^{1}H-^{1}H COSY 90° spectrum



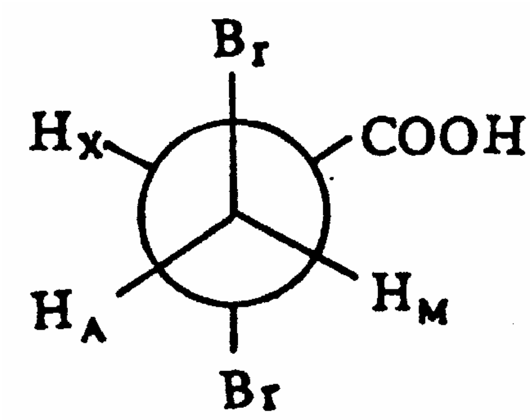


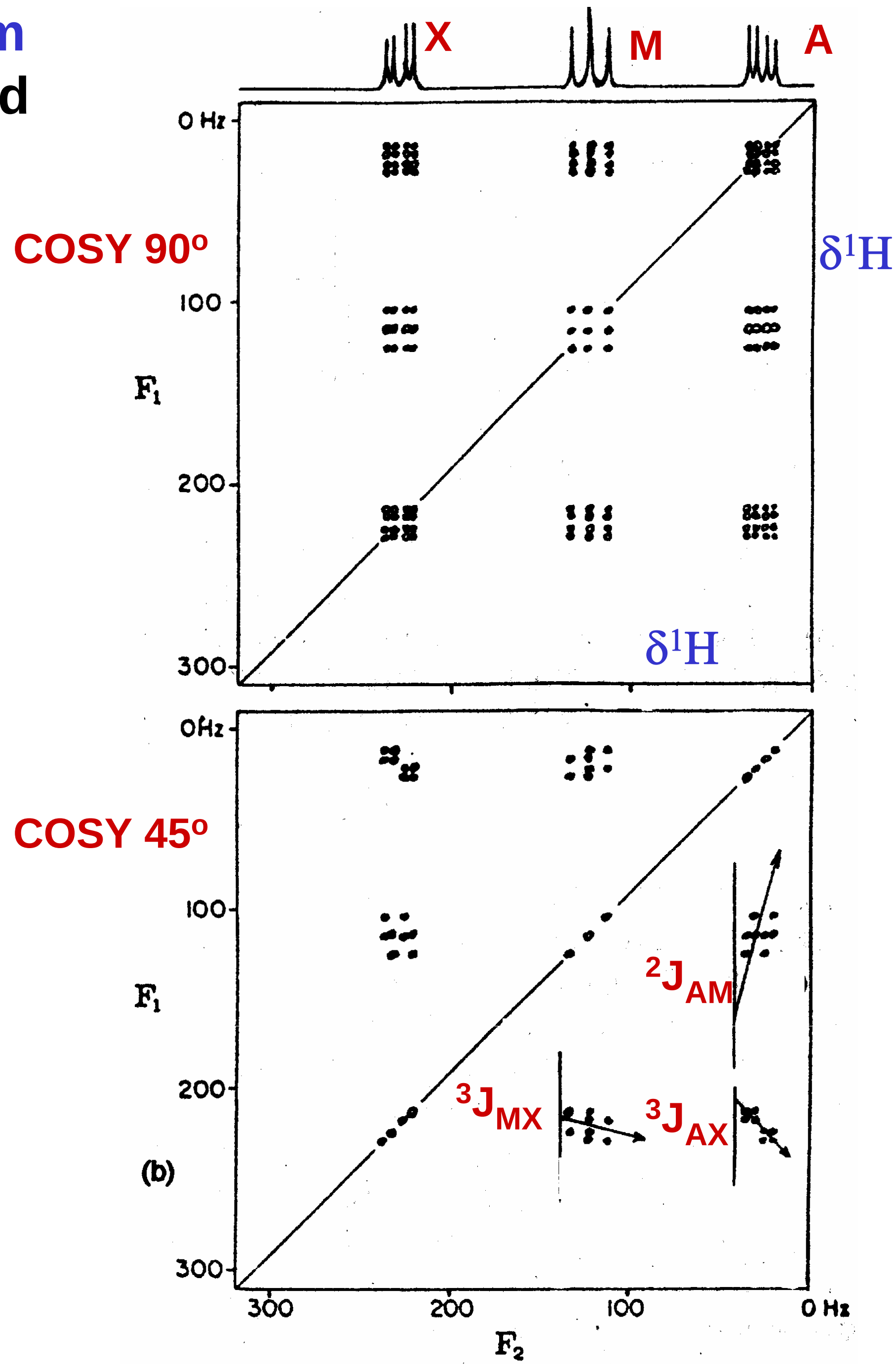
2D ^1H-^1H COSY 90° spectrum



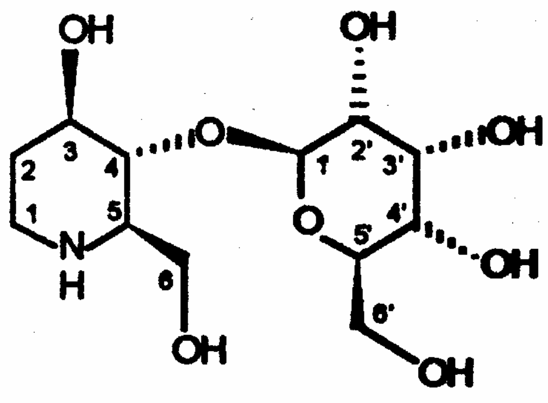


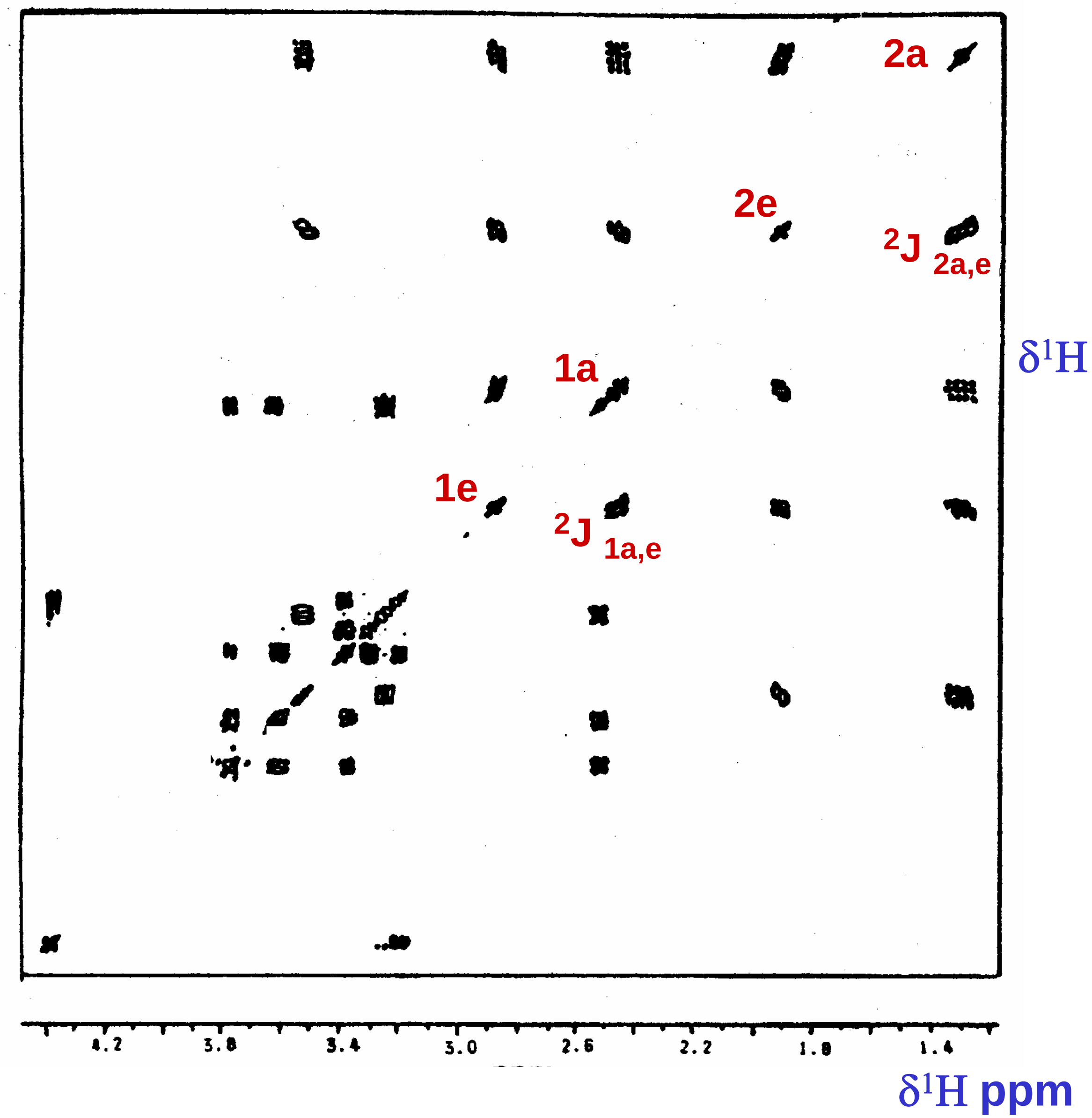
2D ^{1}H-^{1}H COSY 45° spectrum of Dibromo - Propionic Acid



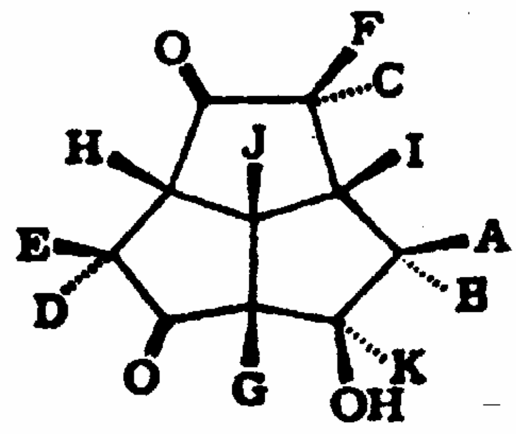


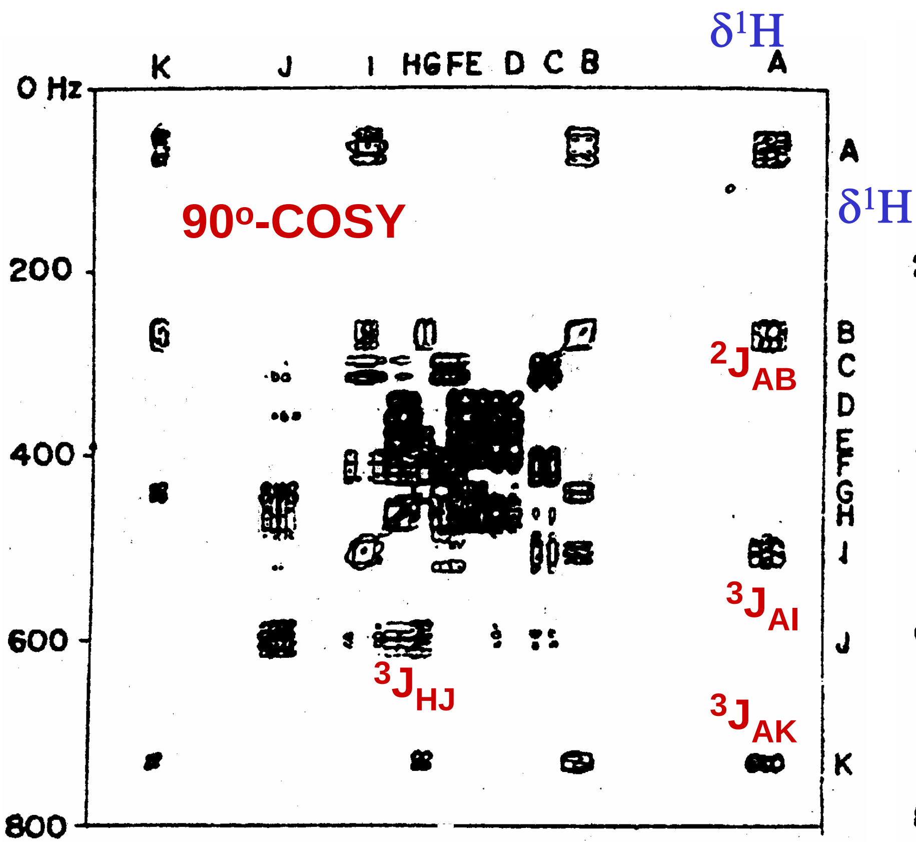
2D ^{1}H-^{1}H COSY 45° experiment

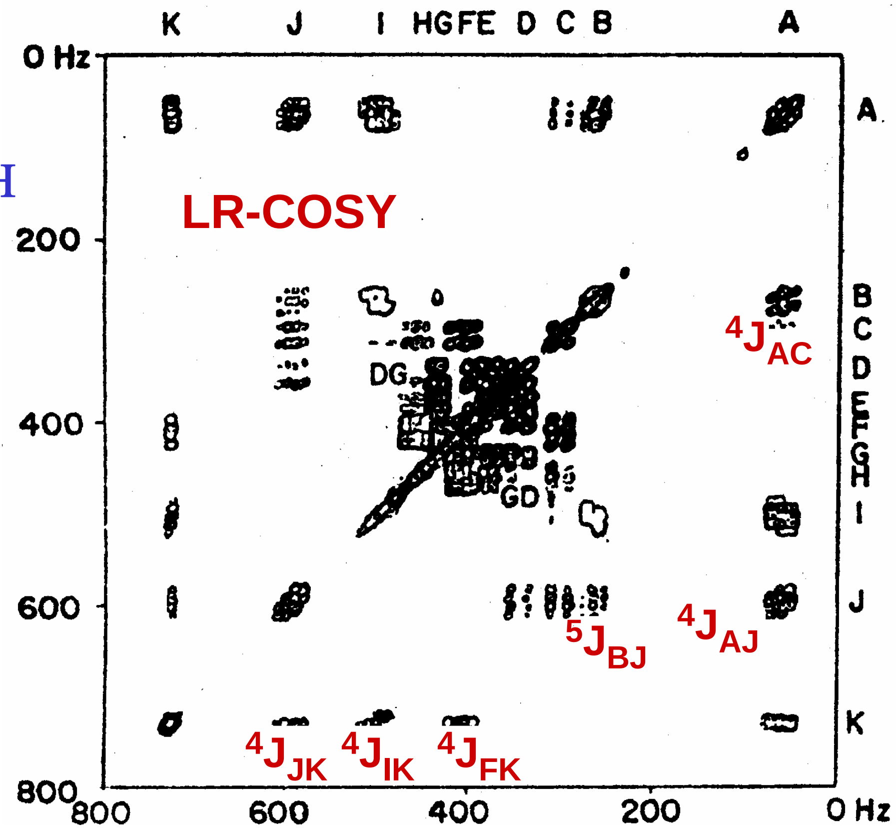




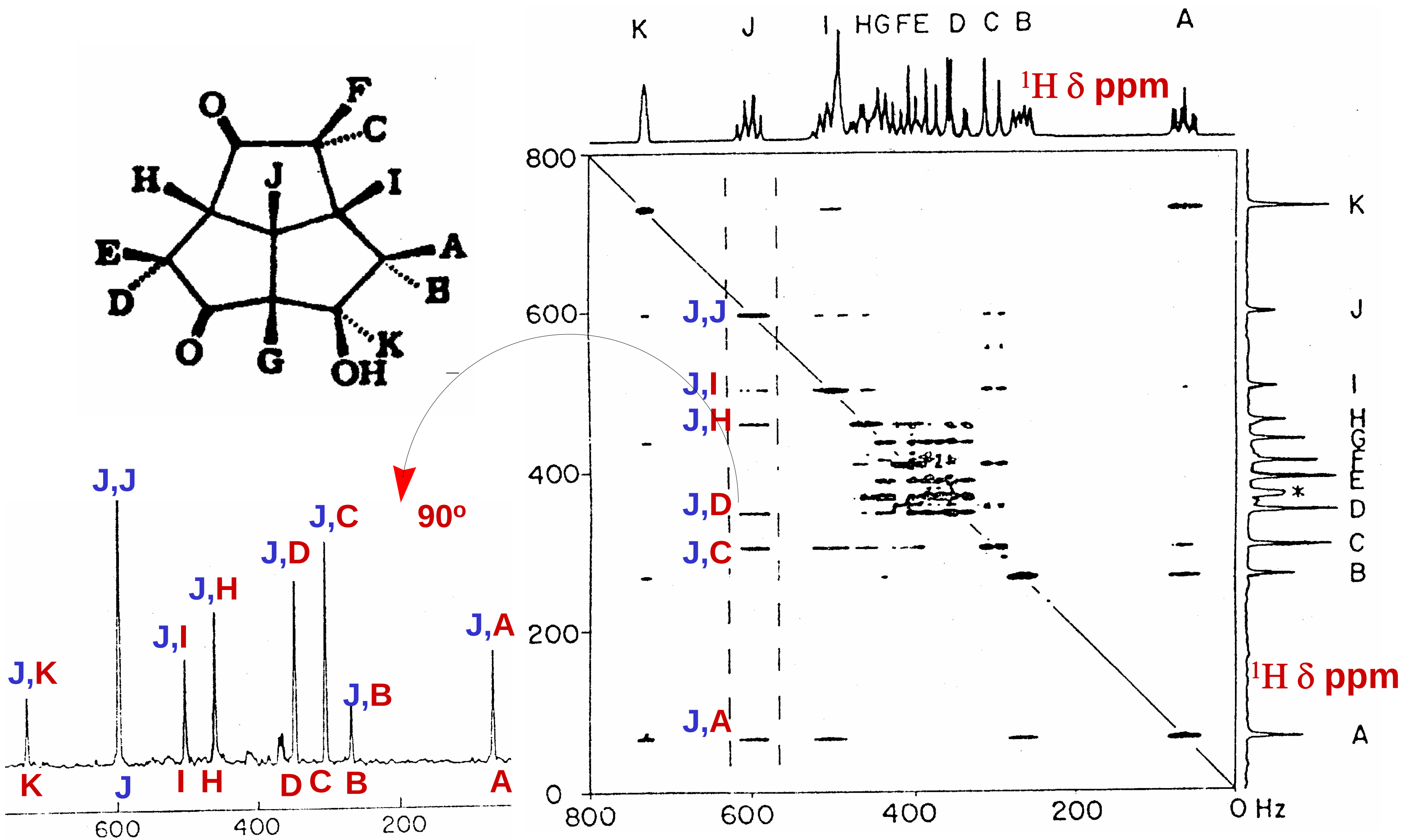
2D ^1H-^1H Long- Range COSY of tricyclodecane





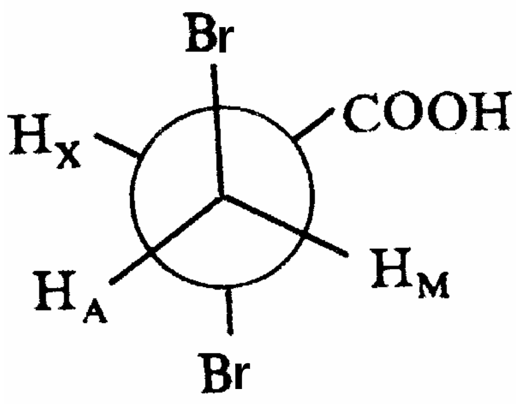


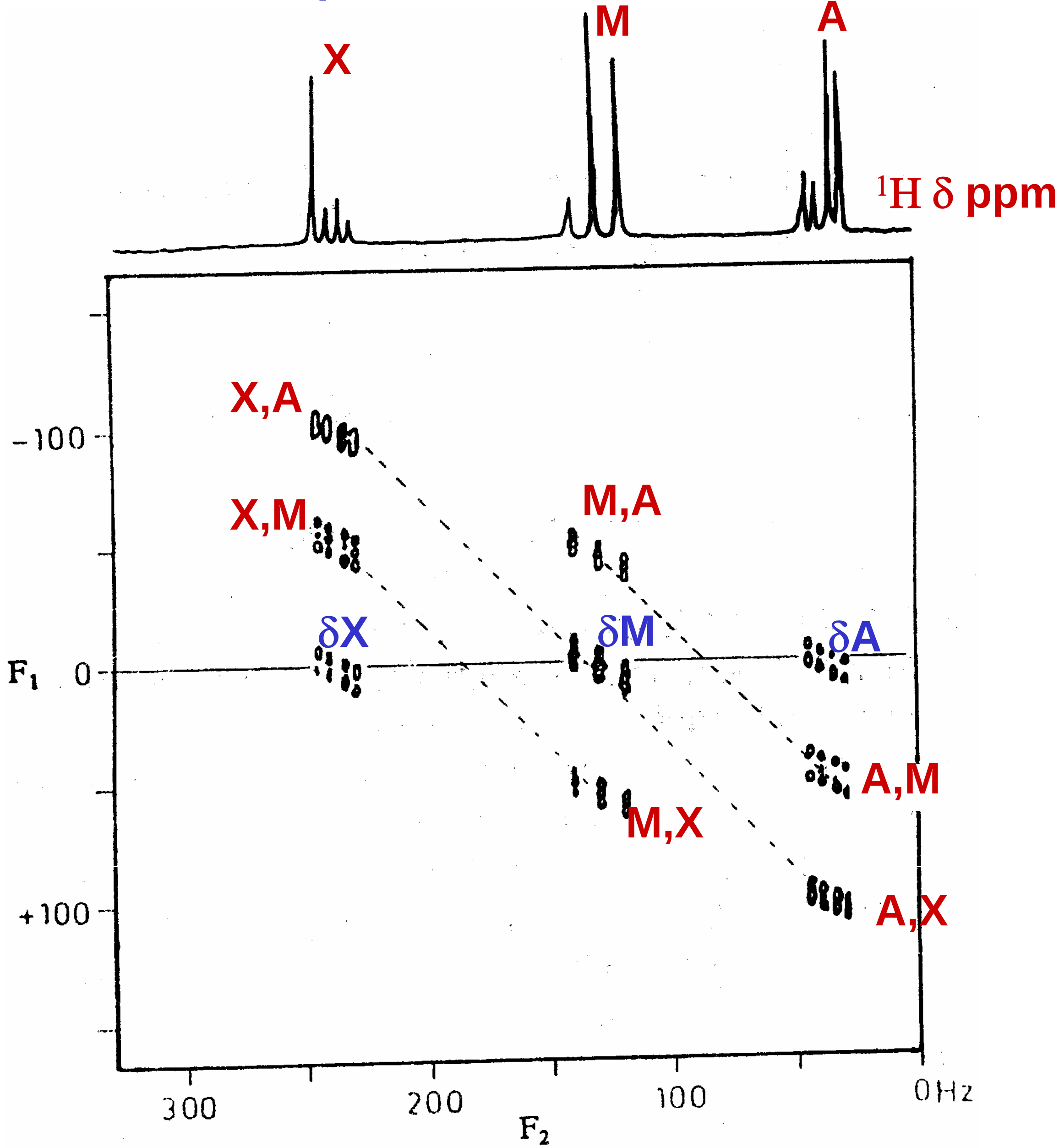
2D ^{1}H-^{1}H HD - (Homonuclear Decoupling) COSY of tricyclodecane



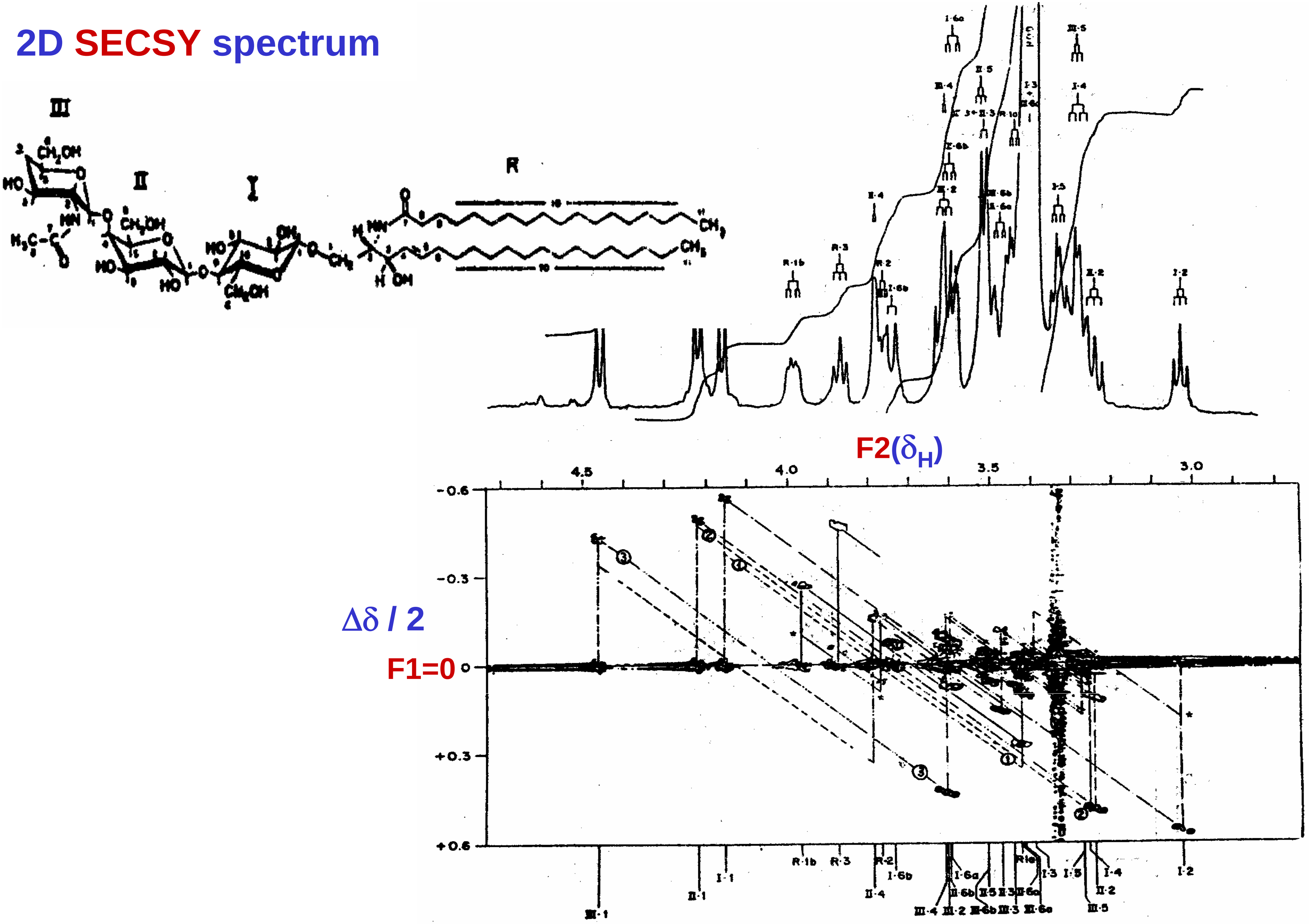
projection of F_1 axis

2D ^{1}H-^{1}H SE (Spin Echo)- COSY spectrum of Dibromo - Propionic Acid

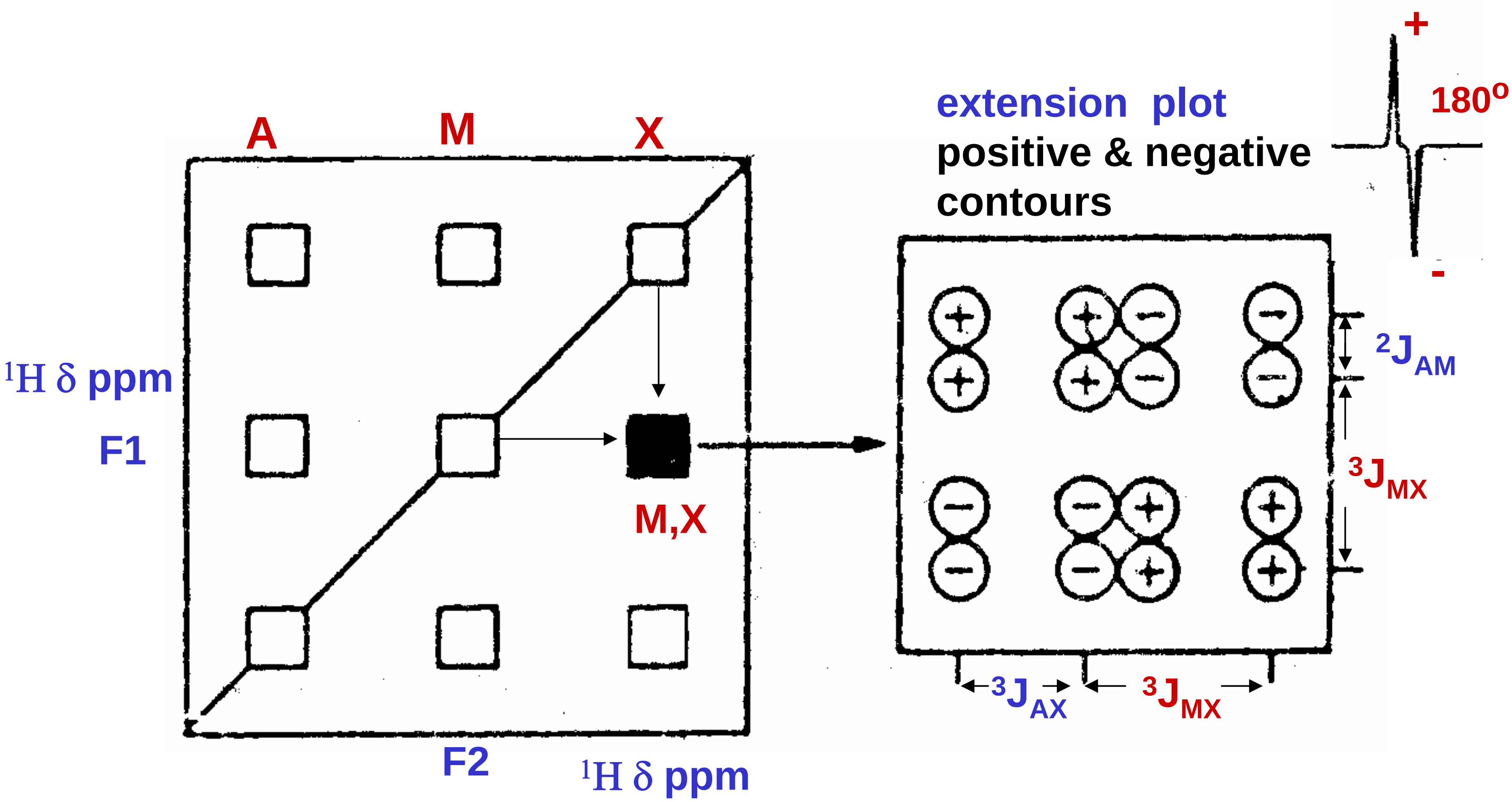




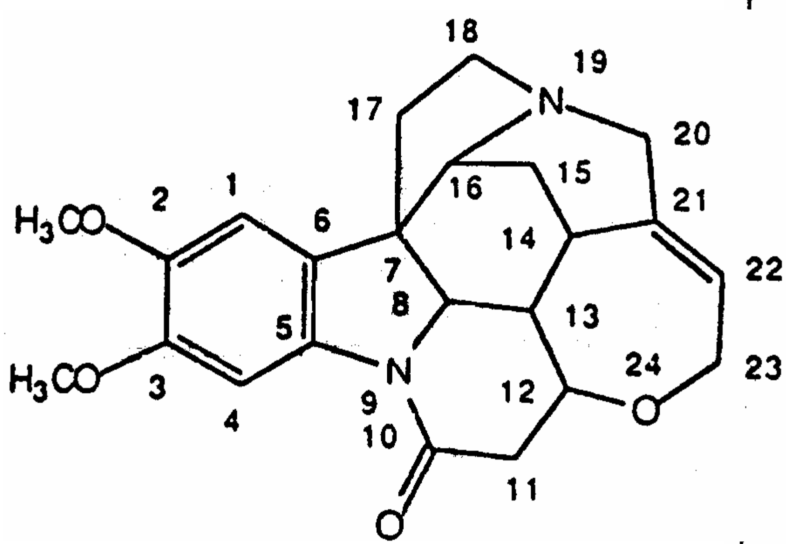
2D SECSY spectrum

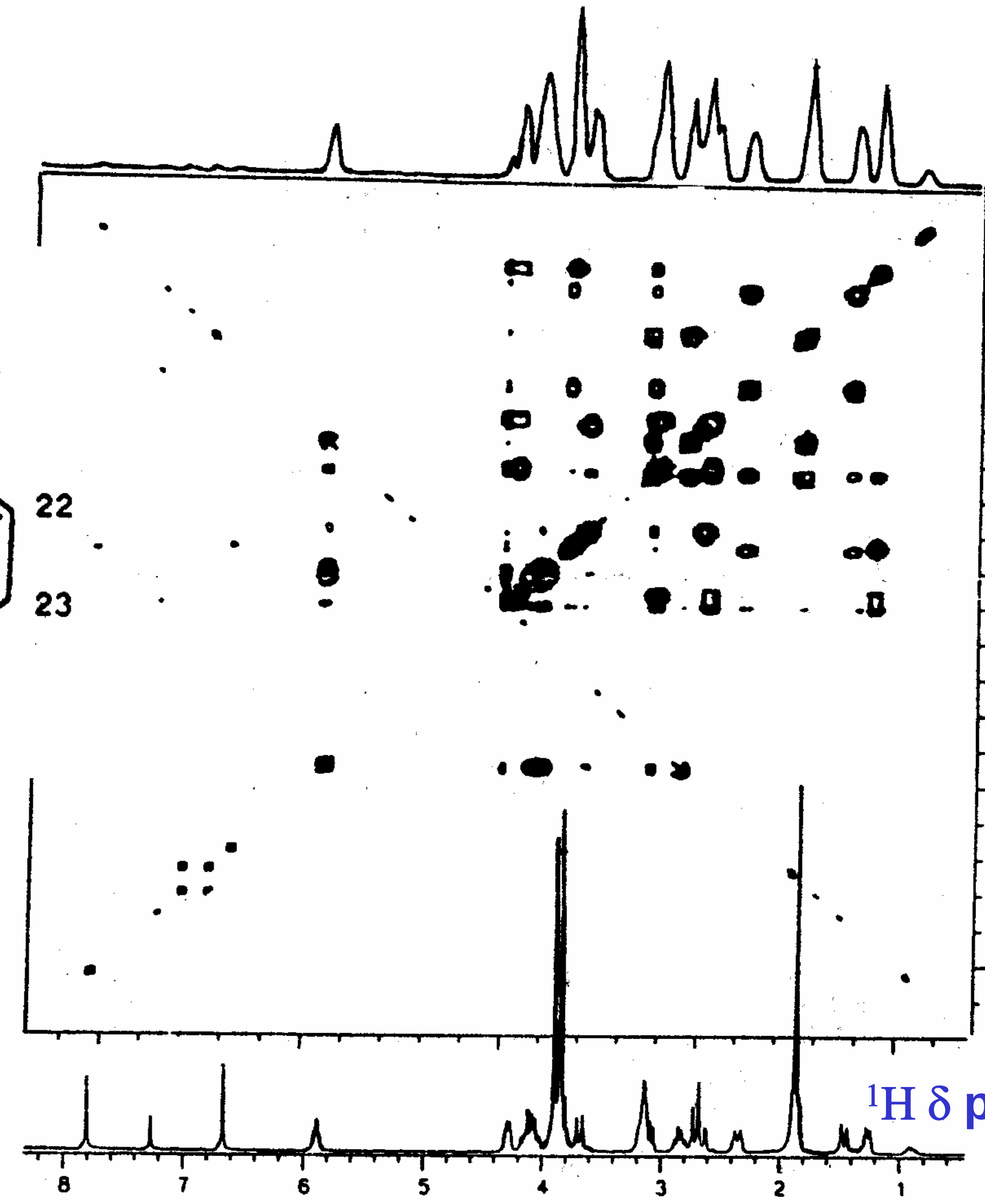


2D ^1H-^1H DQF- COSY (Double Quantum Filtered Correlation Spectroscopy)



2D ^1H-^1H DQF- COSY spectrum

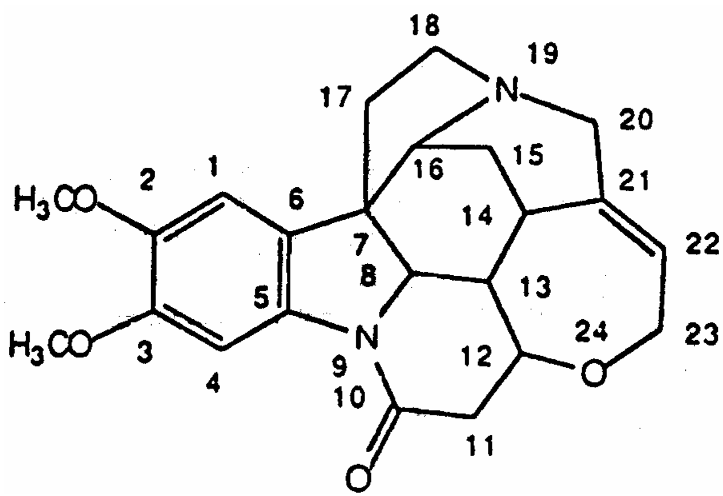


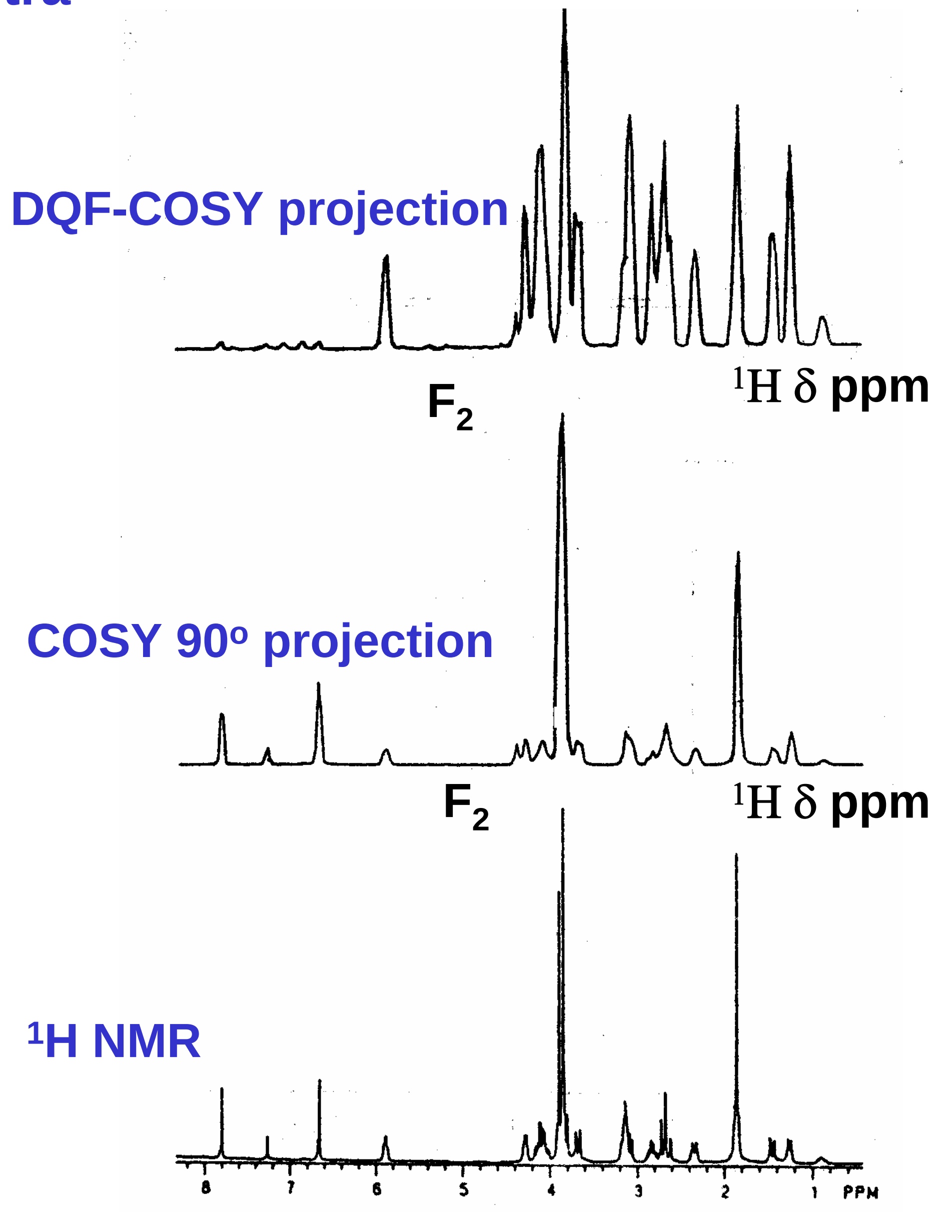


δ_H

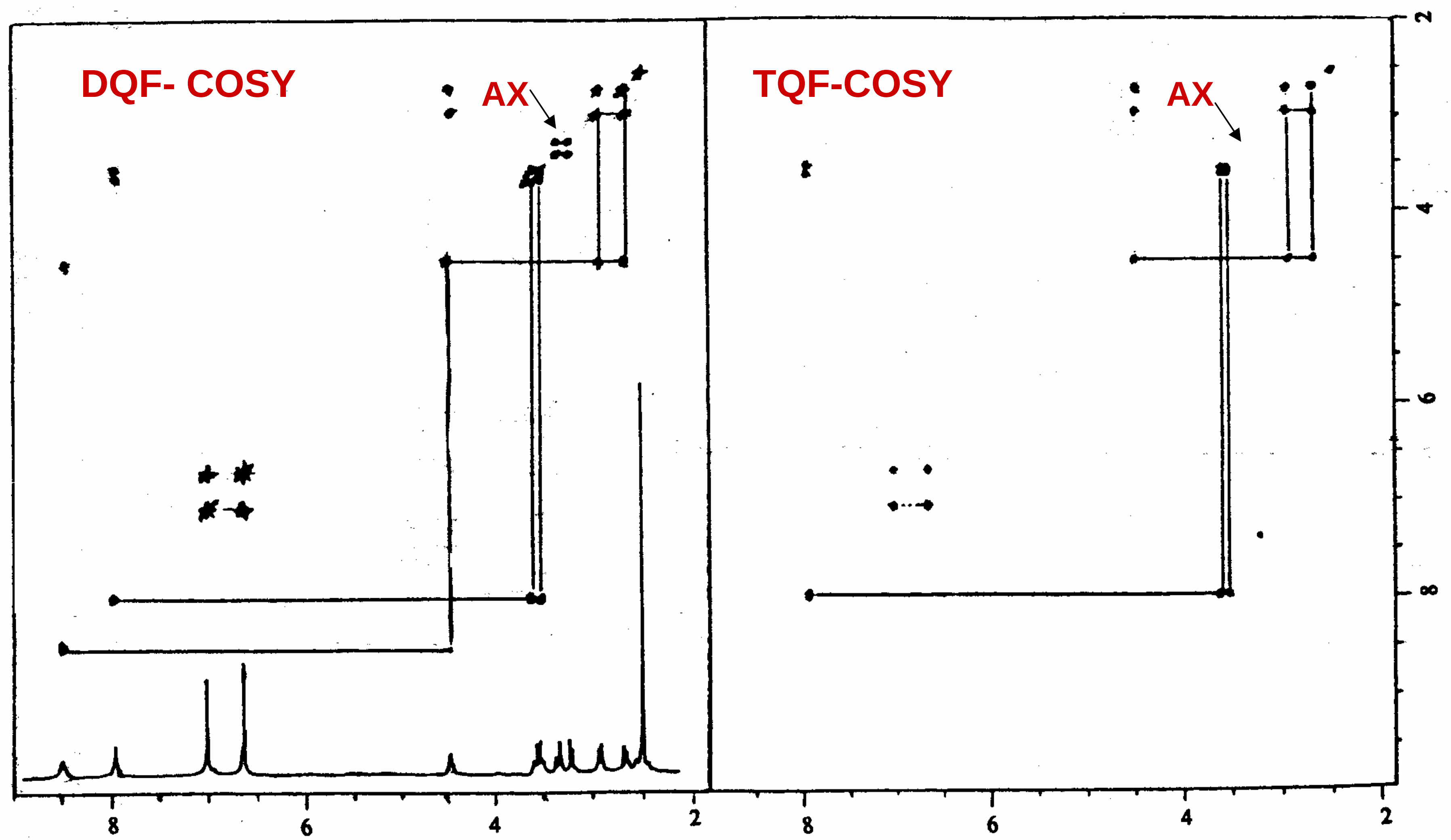
^1H δ ppm

2D ^1H-^1H DQF- COSY spectra

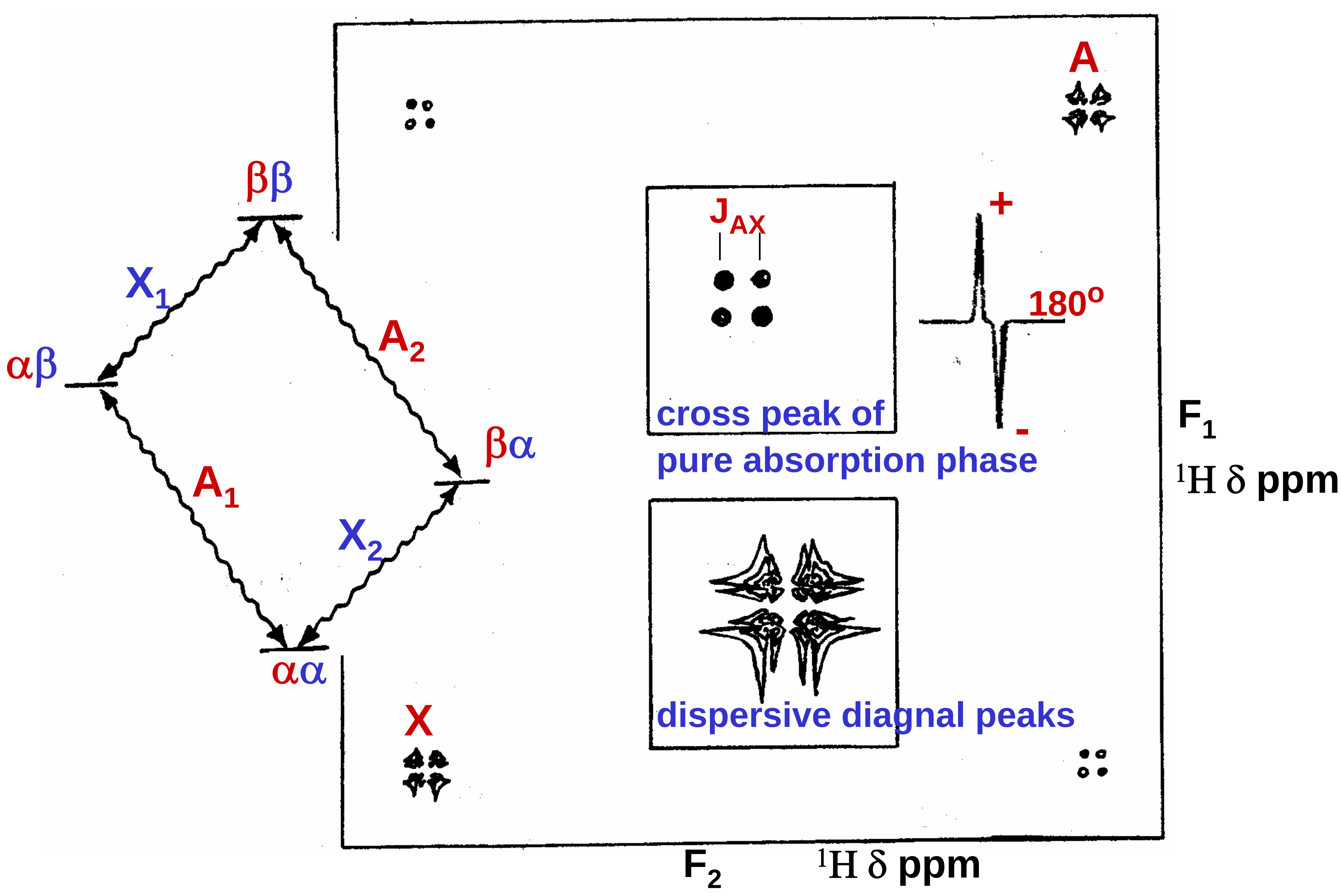




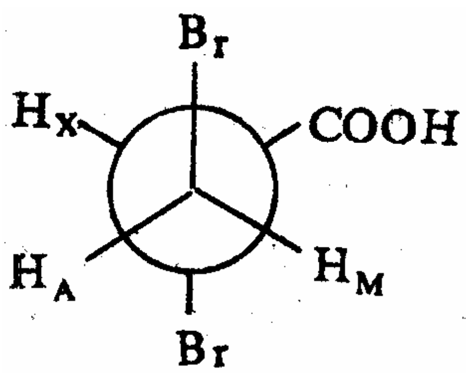
Comparision of DQF- COSY and TQF- COSY spectra

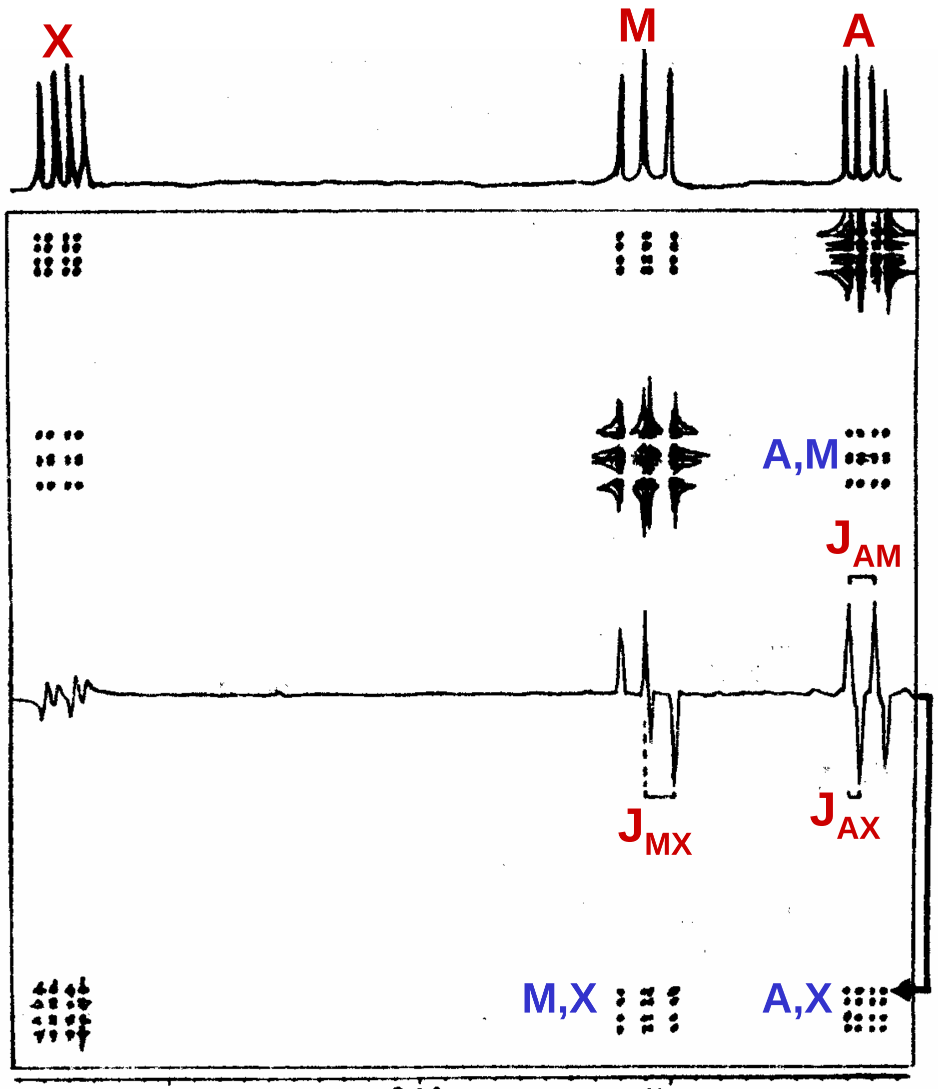


2D ^1H-^1H PH- COSY (Phase sensitive cosy) experiment

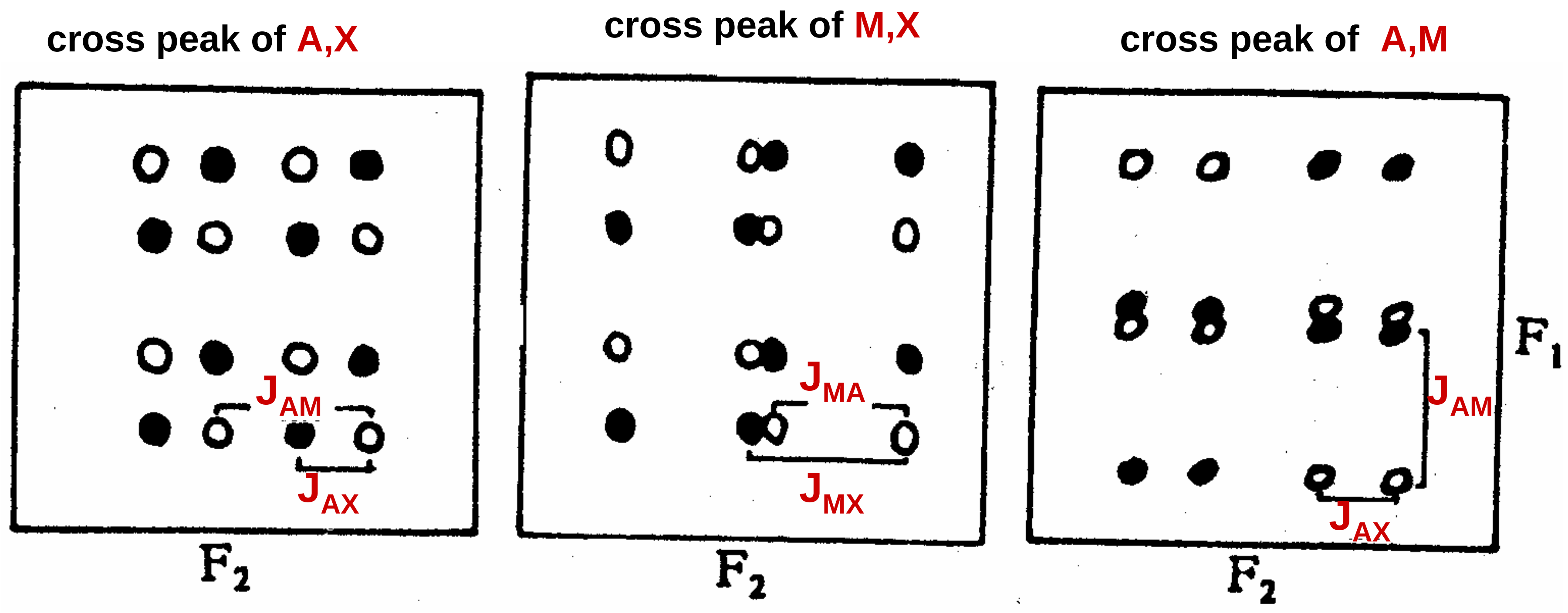


2D ^{1}H-^{1}H Phase sensitive COSY spectrum of Dibromopropionic Acid

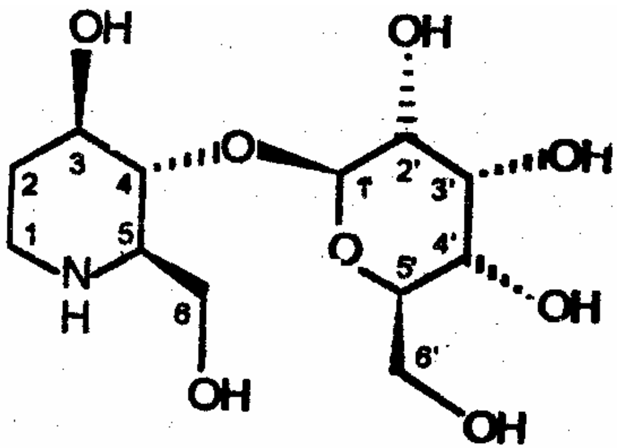


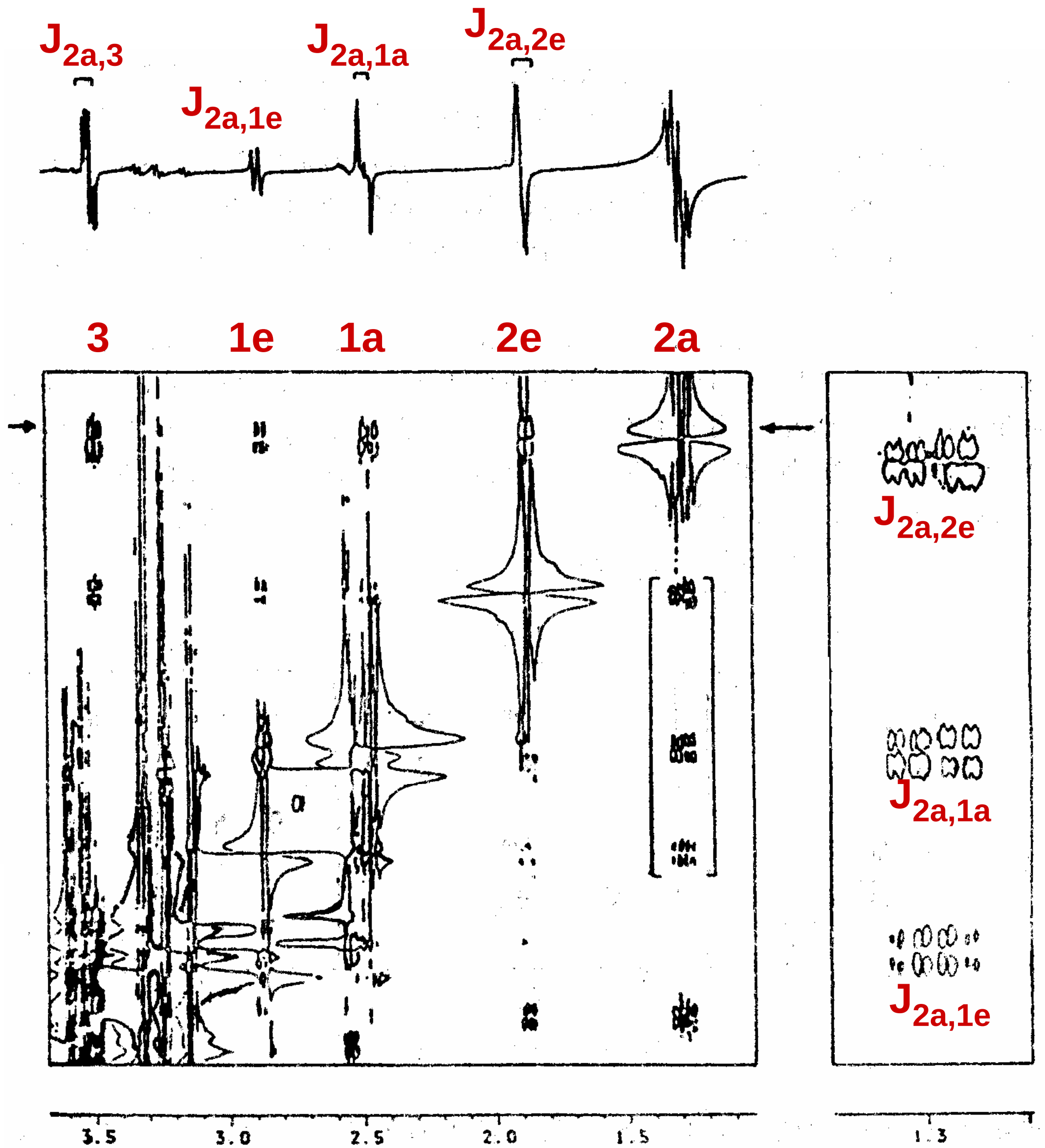


2D ^1H-^1H Phase sensitive COSY spectrum for AMX system
(positive and negative contours)



2D ^{1}H-^{1}H Phase sensitive COSY spectrum





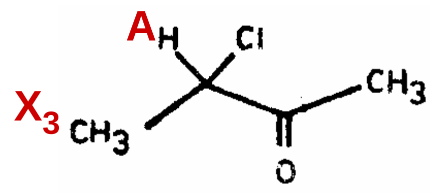
Comparision of phase sensitive COSY and ^{1}H-^{1}H COSY spectra

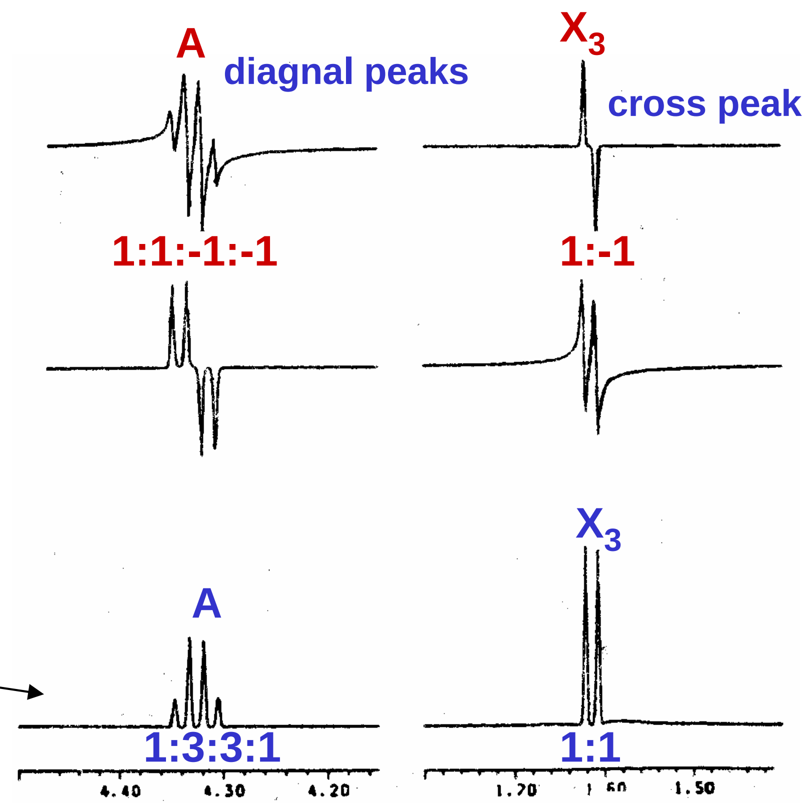
antiphase triangle
(for COSY):

1
1 −1
1 0 −1
1 1 −1 −1
1 2 0 −2 −1
1 3 2 −2 −3 −1

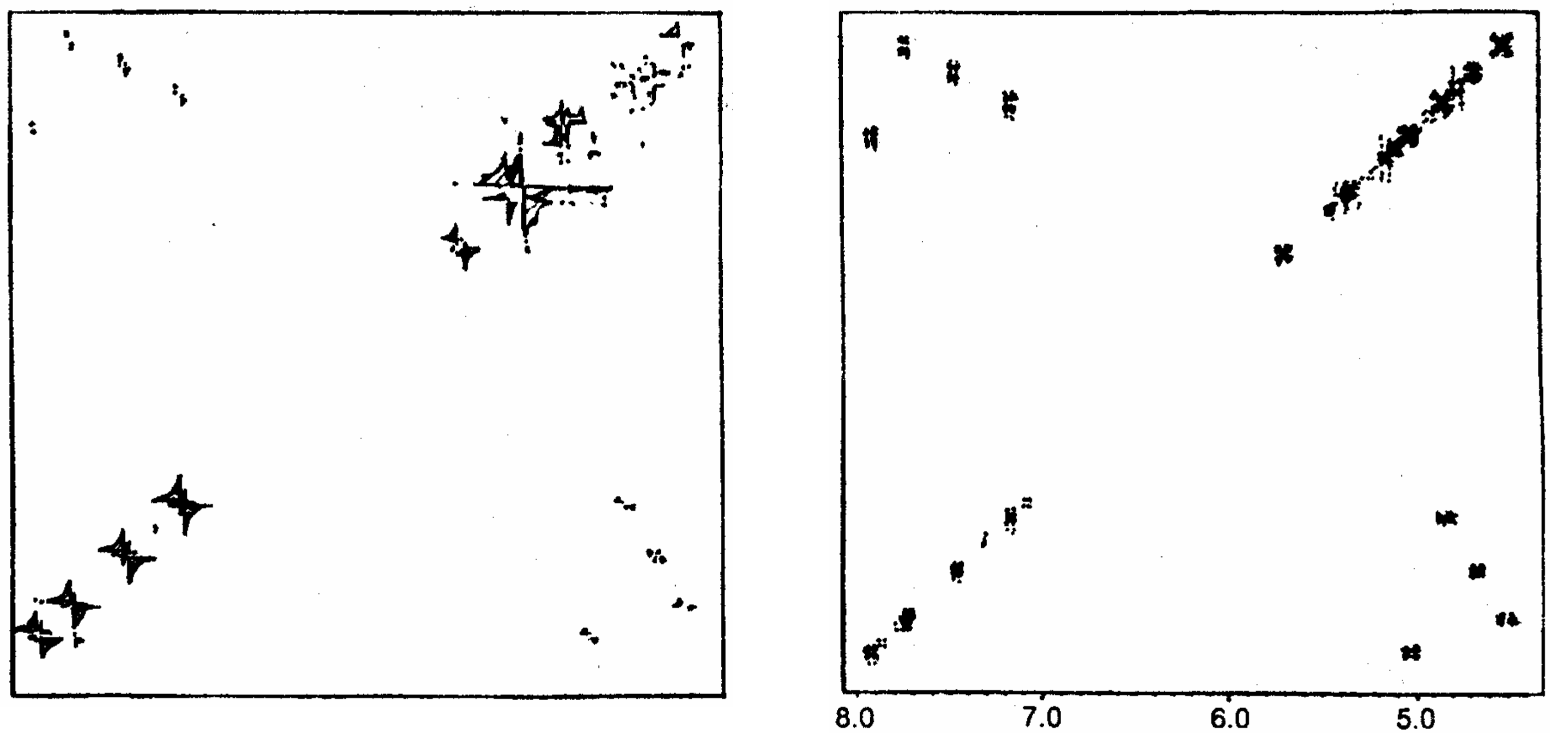
Pascal's triangle
(for equivalent nuclei in normal spectra):

1
1 1
1 2 1
1 3 3 1
1 4 6 4 1
1 5 10 10 5 1

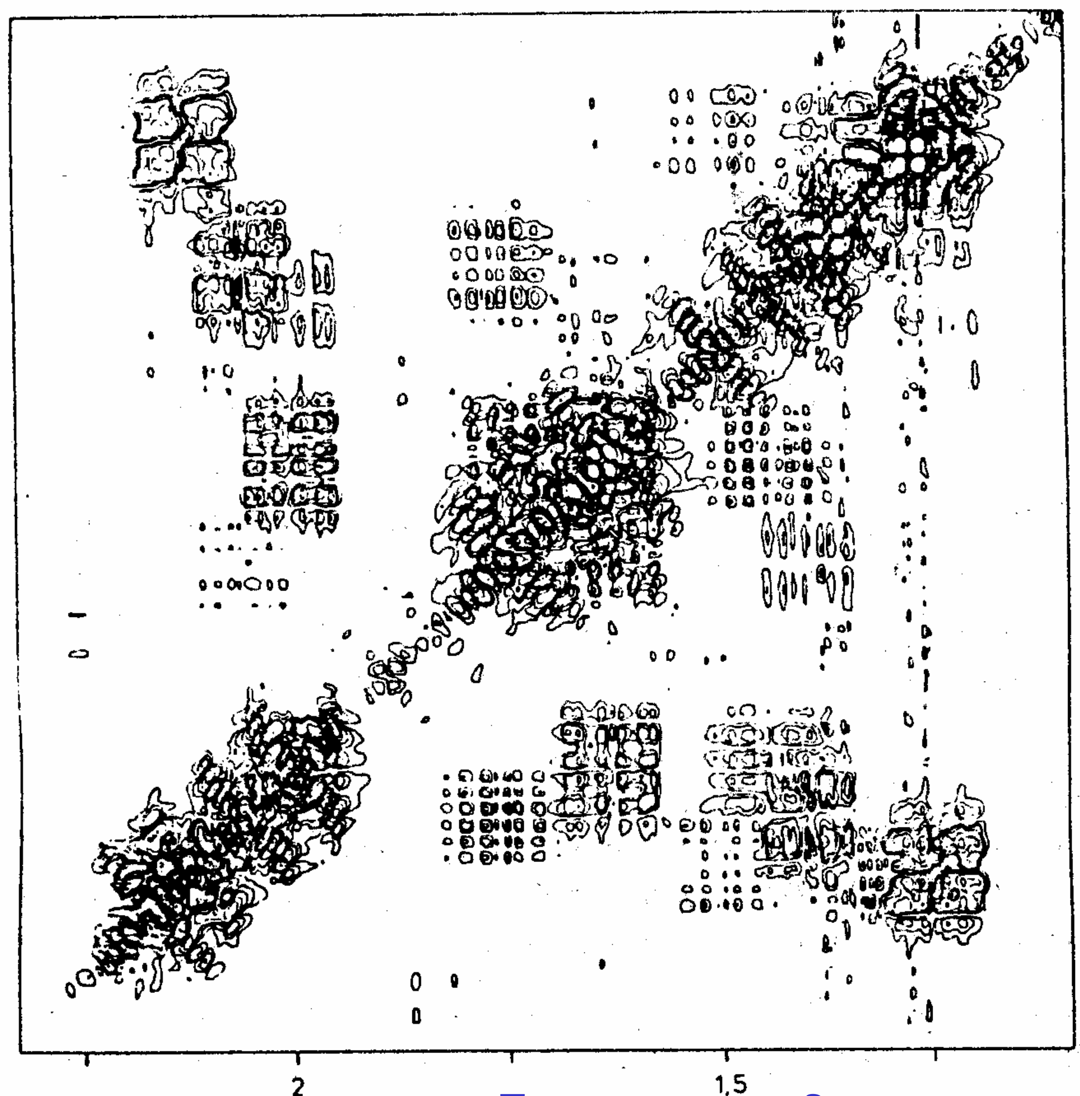




Comparision of PHase sensitive COSY and DQFPH- COSY spectra



Part of the DQF- PH- COSY spectrum of Cycolsporin



F_1

δ_H

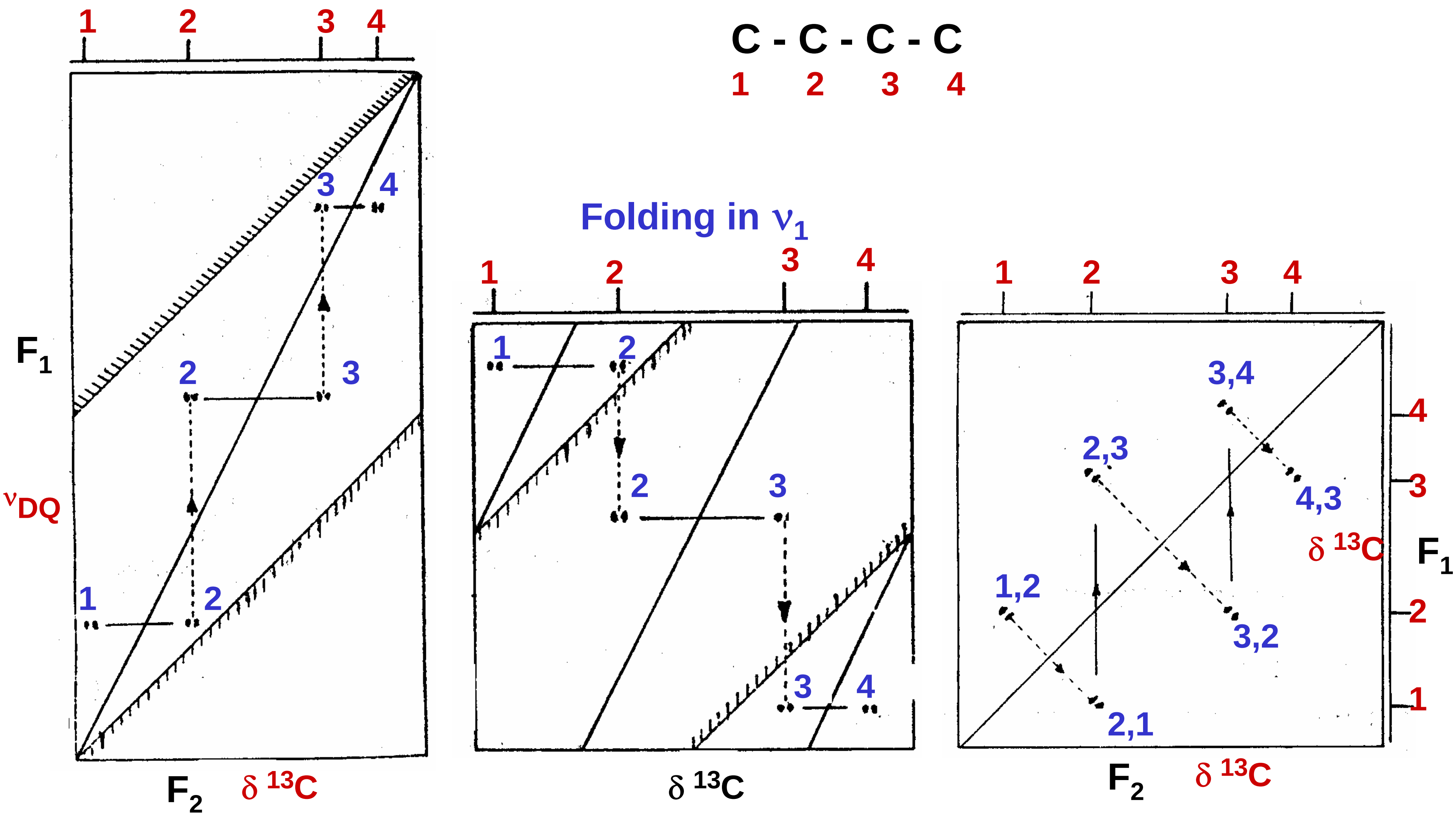
F_2

δ_H ppm

^{13}C-^{13}C 2D Correlations:

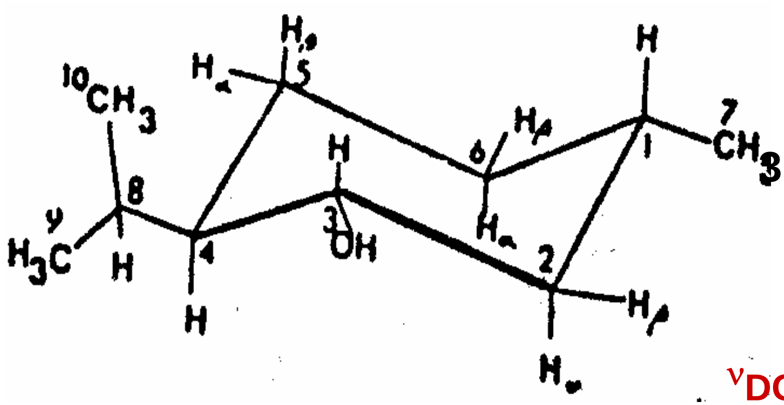
2D INADEQUATE (Incredible Natural Abundance DoublE QUantum Transfer Experiments)

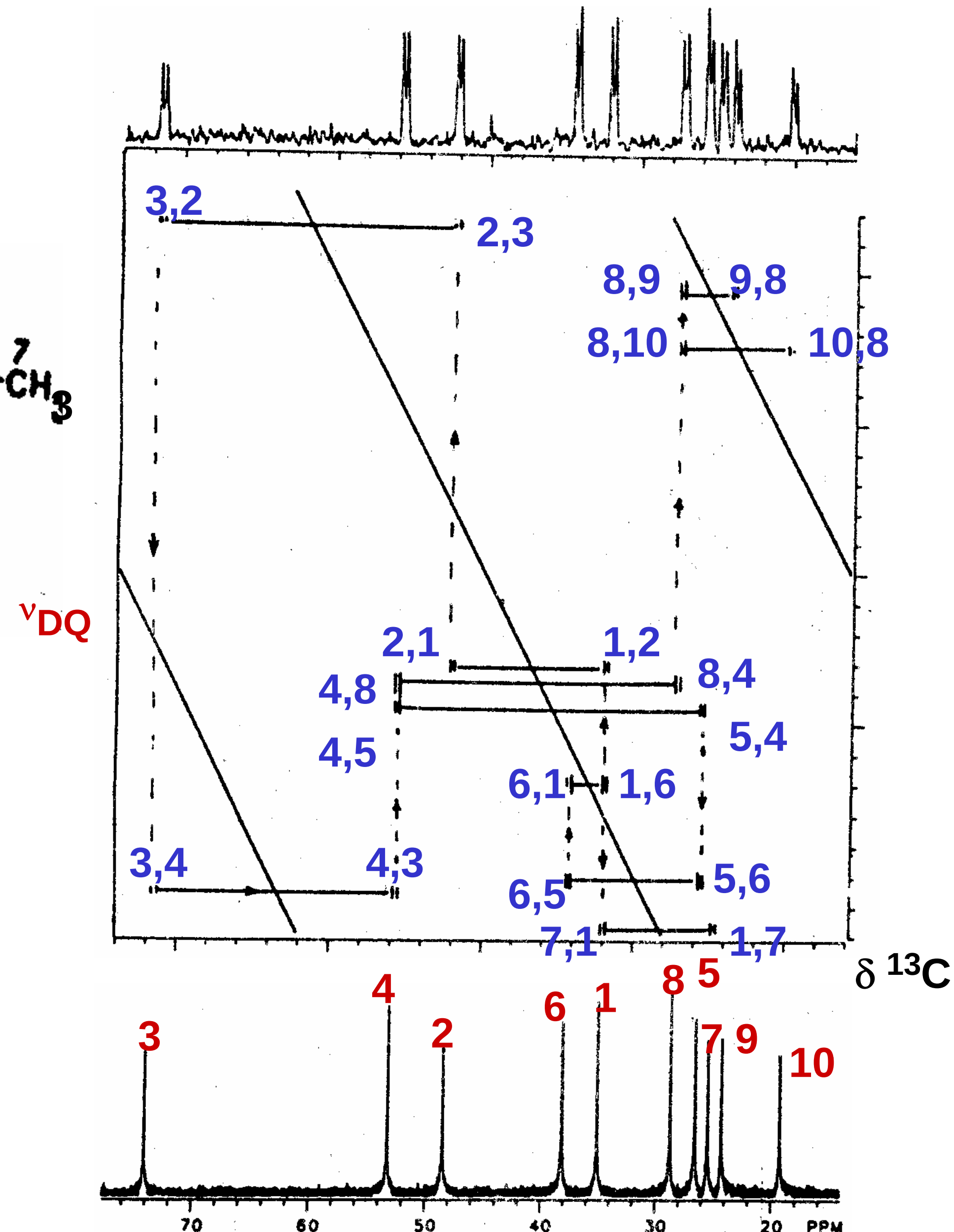
C - C - C - C
1 2 3 4



^{13}C-^{13}C 2D INADEQUATE spectrum of menthol

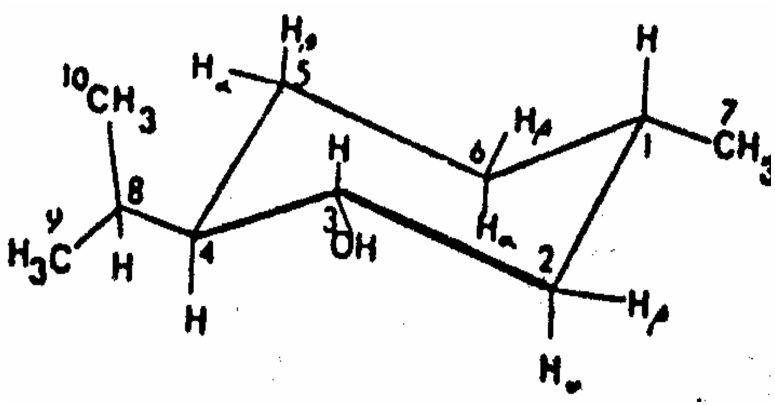
F_1 (ν_{DQ}) F_2 (δ ^{13}C)

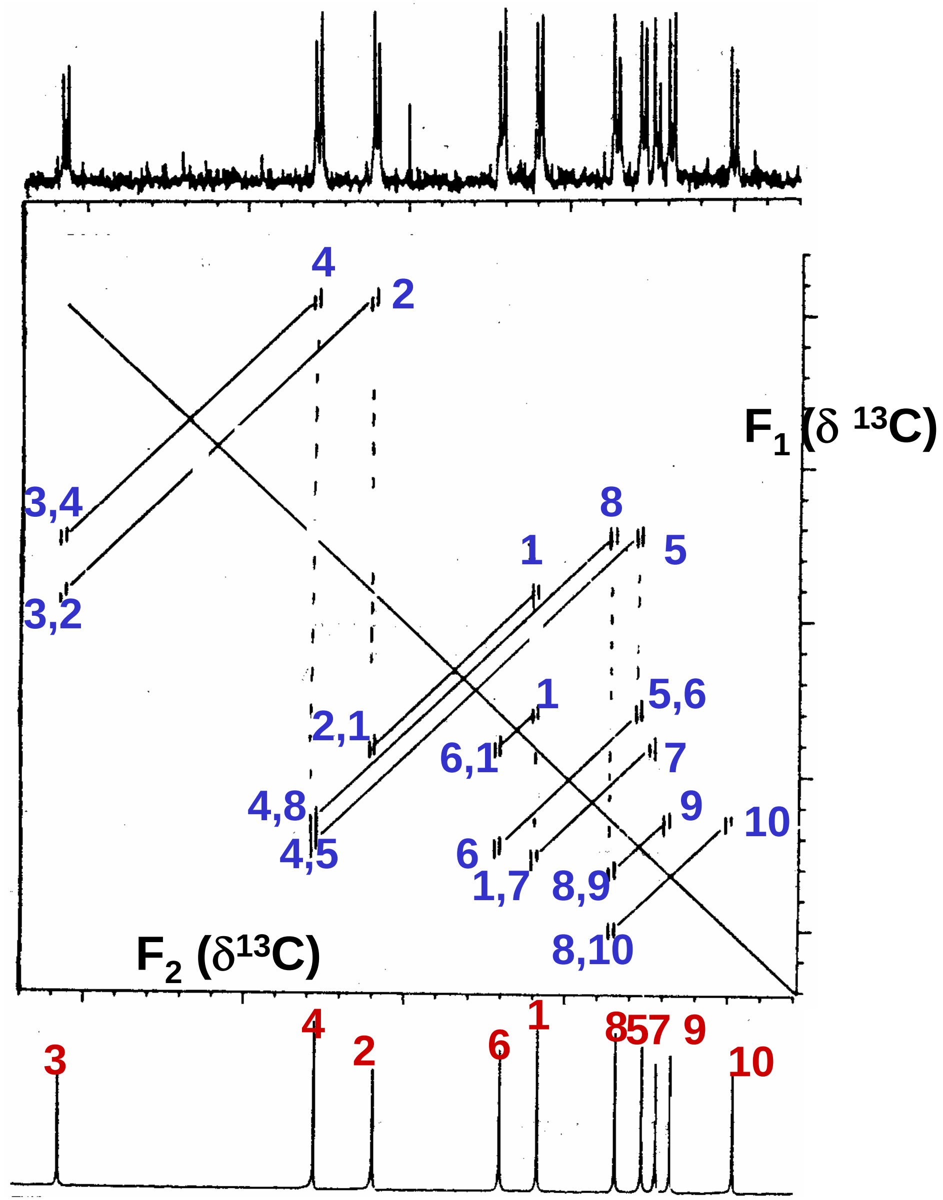




^{13}C-^{13}C 2D INADEQUATE spectrum of menthol

F_1 (δ ^{13}C) F_2 (δ ^{13}C)





Chapter 9

Spectral Analysis of

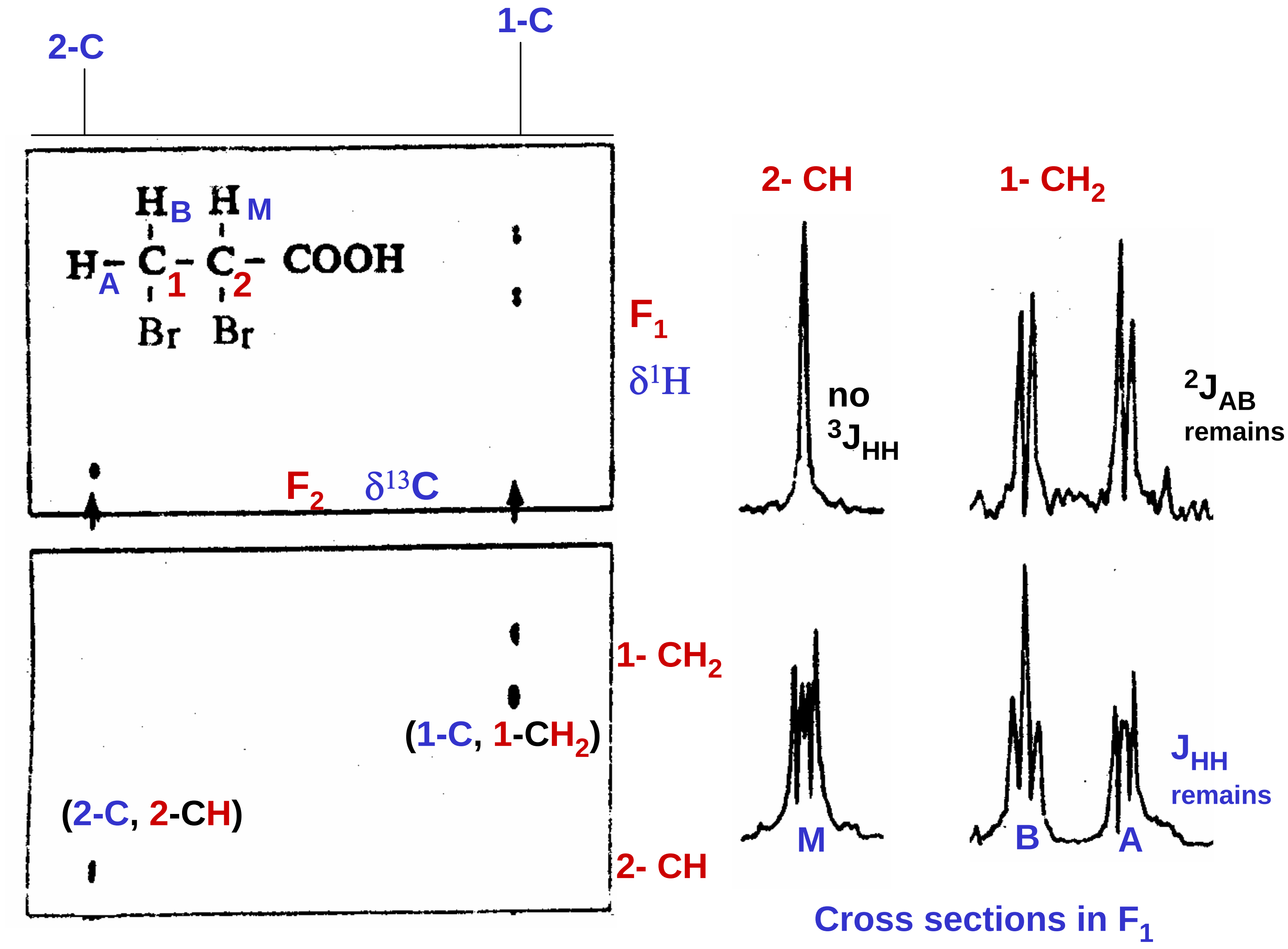
2D Correlation NMR Spectroscopy

Common Heteronuclear 2D

2D chemical shift correlation spectroscopy :

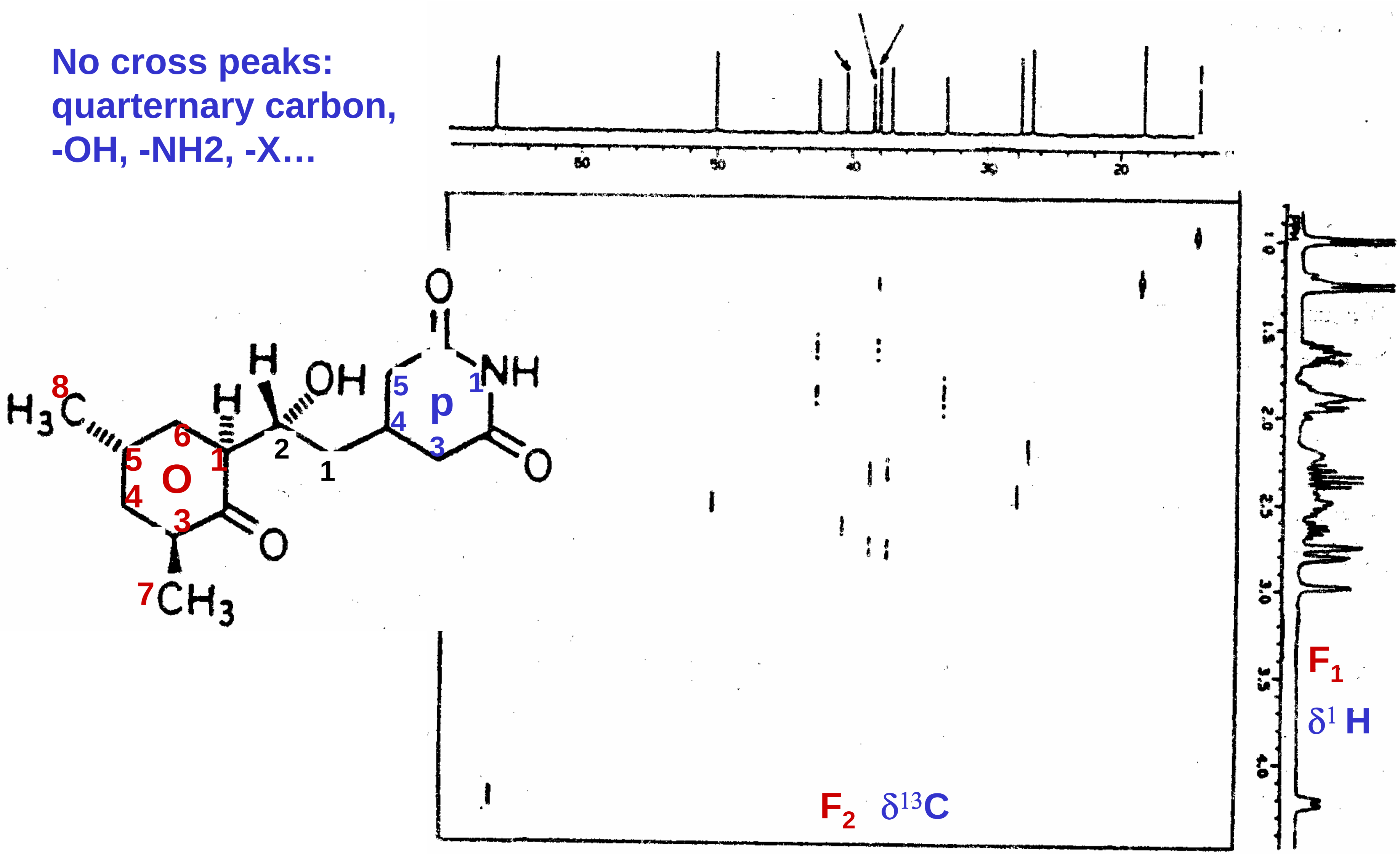
1. 2D ^{13}C-^{1}H COSY (COrrelation SpectroscopY) $^{1}J_{CH}$
2. Proton- detected HETCOR: HMQC inverse experiments (Heteronuclear Multiple Quantum Coherence) $^{1}J_{CH}$
3. 2D COLOC (COrrelation LOng range Coupling) $^{n}J_{CH}$
4. Proton-detected long-range HETCOR : HMBC inverse experiments (Heteronuclear Multiple Bond Coherence) $^{n}J_{CH}$
5. 2D H- H-C Relay correlation spectra $^{2}J_{CH}$

2D ^{13}C-^{1}H COSY spectra ($^{1}J_{CH}$ correlations)



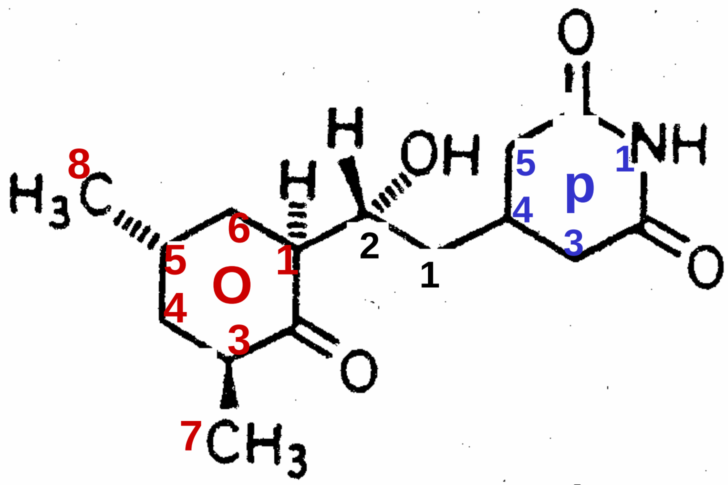
2D ^{13}C-^{1}H COSY spectrum ($^{1}J_{CH}$ correlations)

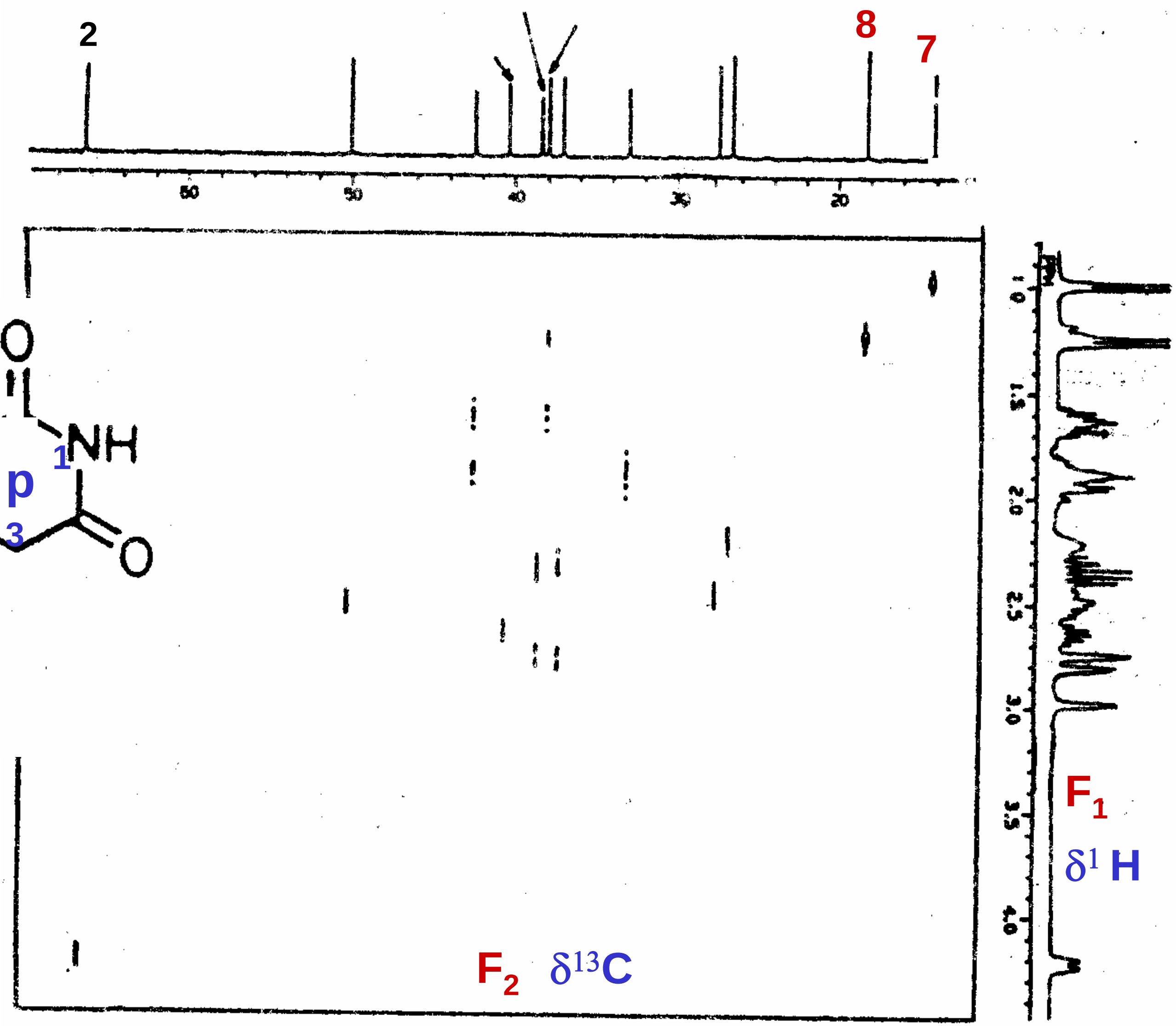
No cross peaks:
quarternary carbon,
-OH, -NH2, -X…



2D ^{13}C-^{1}H COSY spectrum ($^{1}J_{CH}$ correlations)

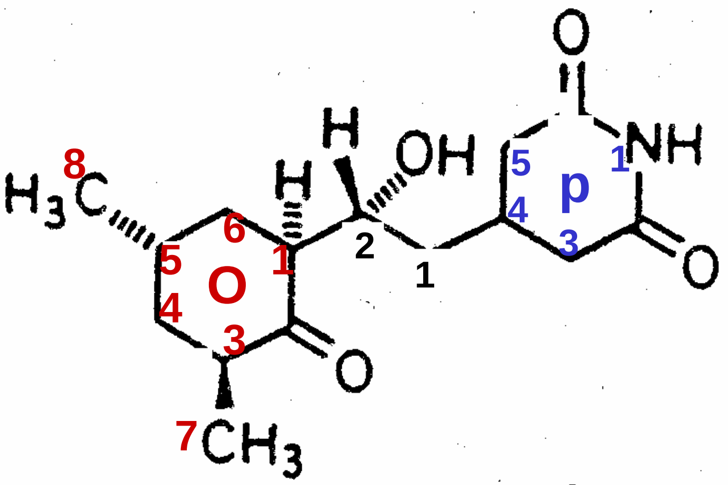
No cross peaks:
quarternary carbon,
-OH, -NH2, -X…

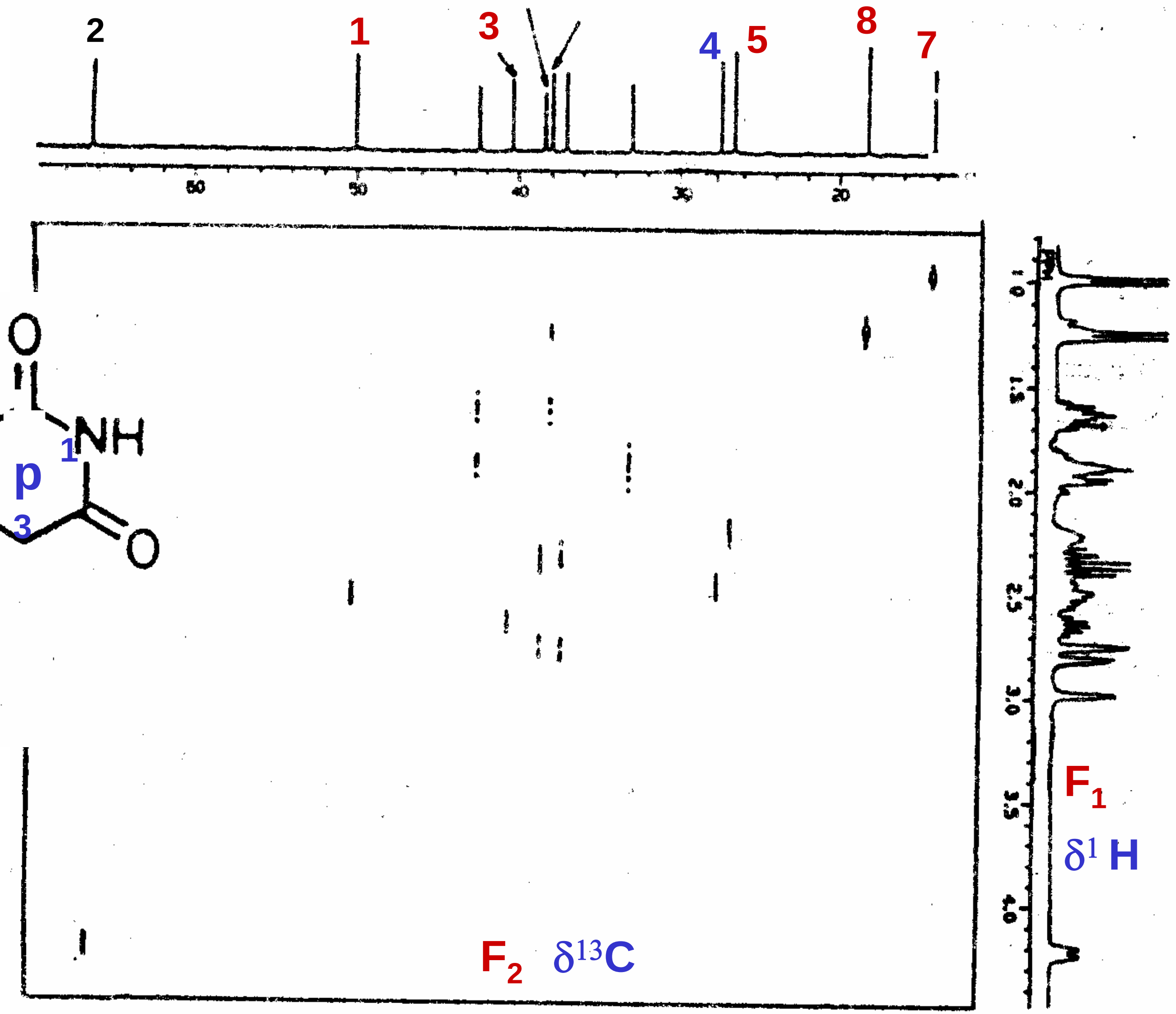




2D ^{13}C-^{1}H COSY spectrum ($^{1}J_{CH}$ correlations)

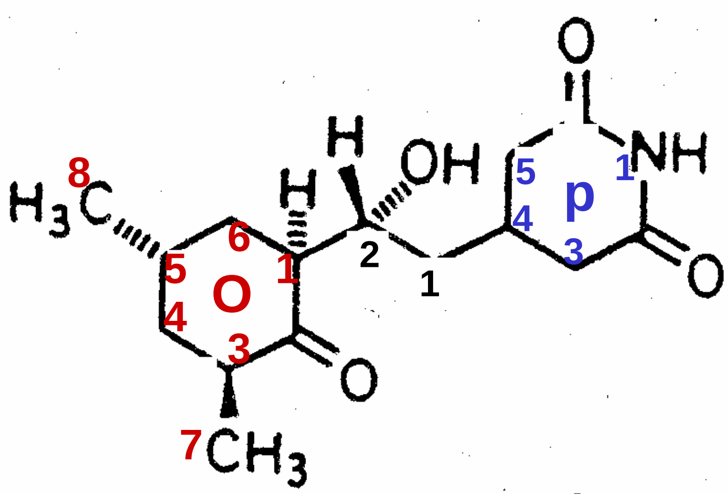
No cross peaks: quarternary carbon, -OH, -NH2, -X…

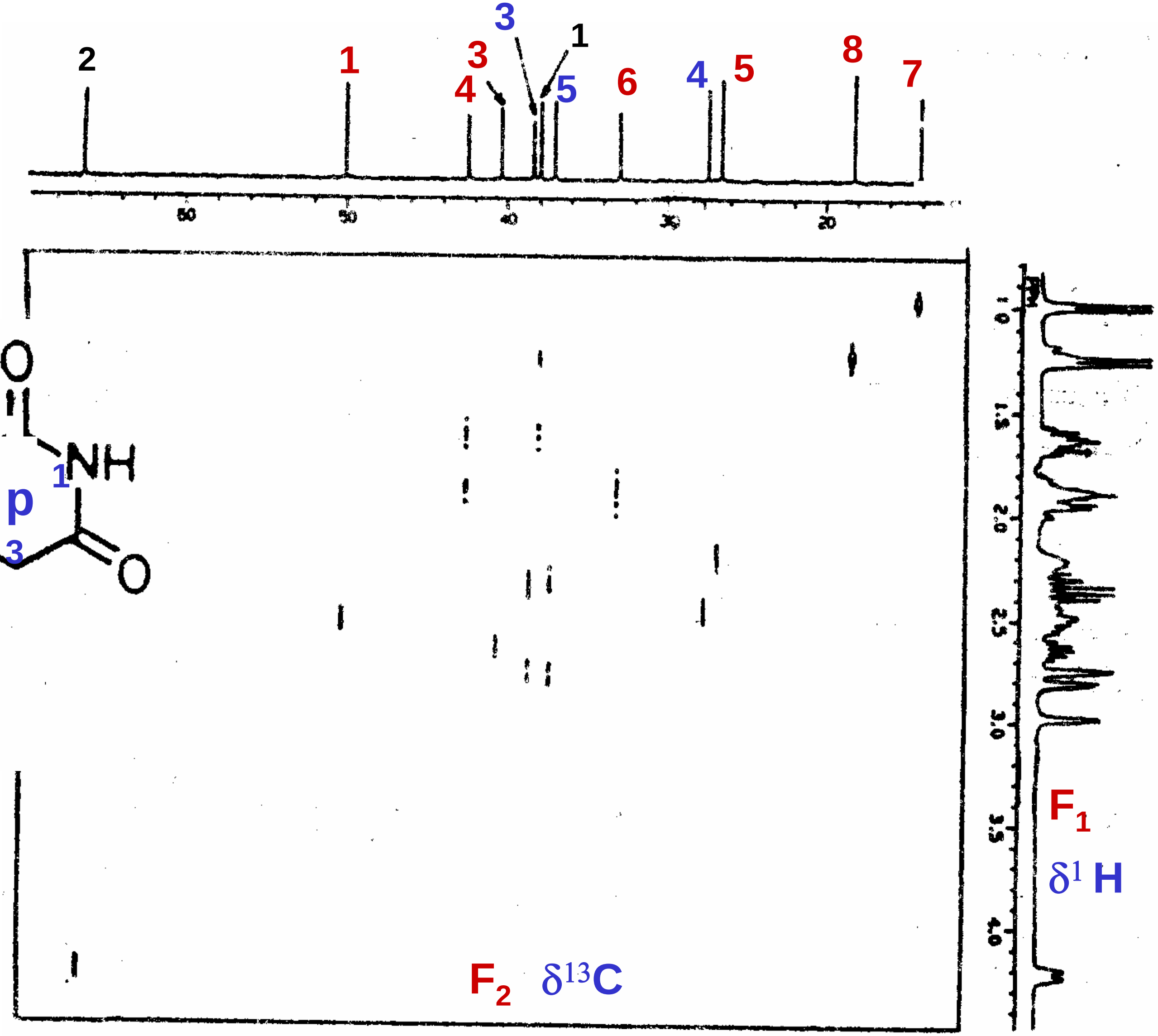




2D ^{13}C-^{1}H COSY spectrum ($^{1}J_{CH}$ correlations)

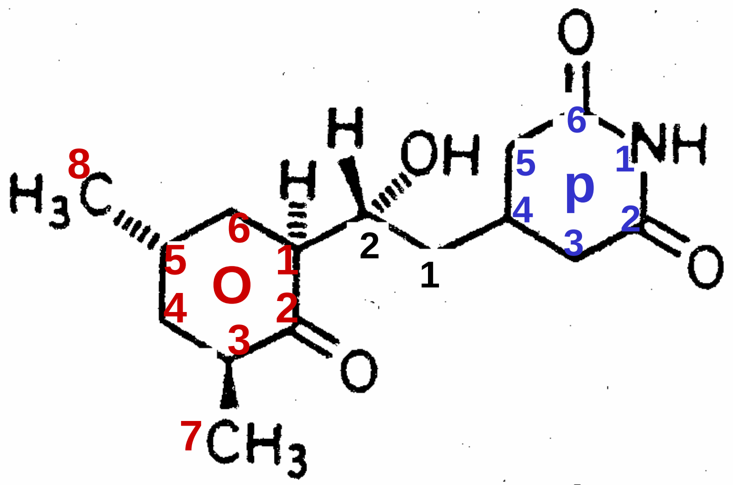
No cross peaks:
quarternary carbon,
-OH, -NH2, -X…

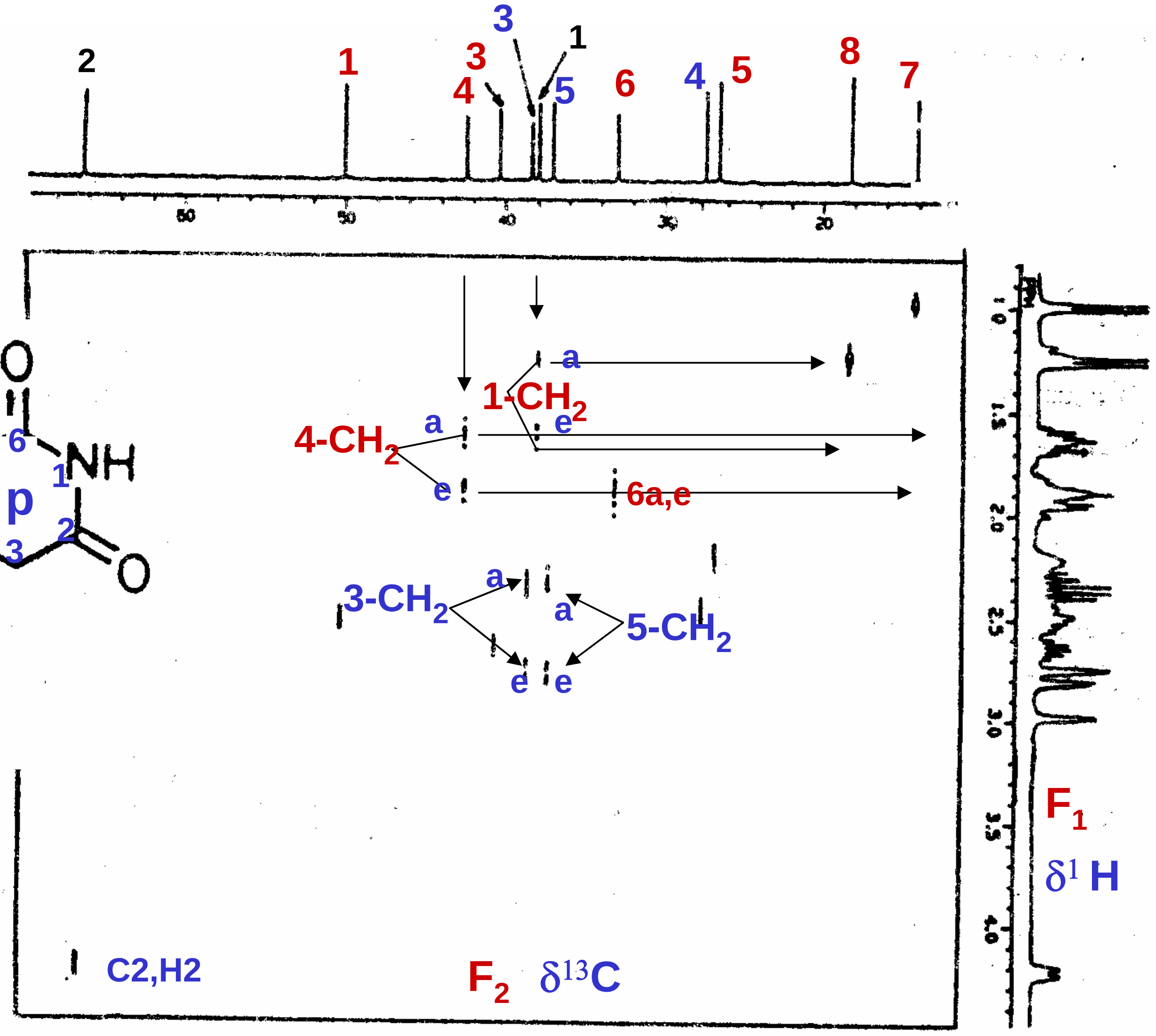




2D ^{13}C-^{1}H COSY spectrum ($^{1}J_{CH}$ correlations)

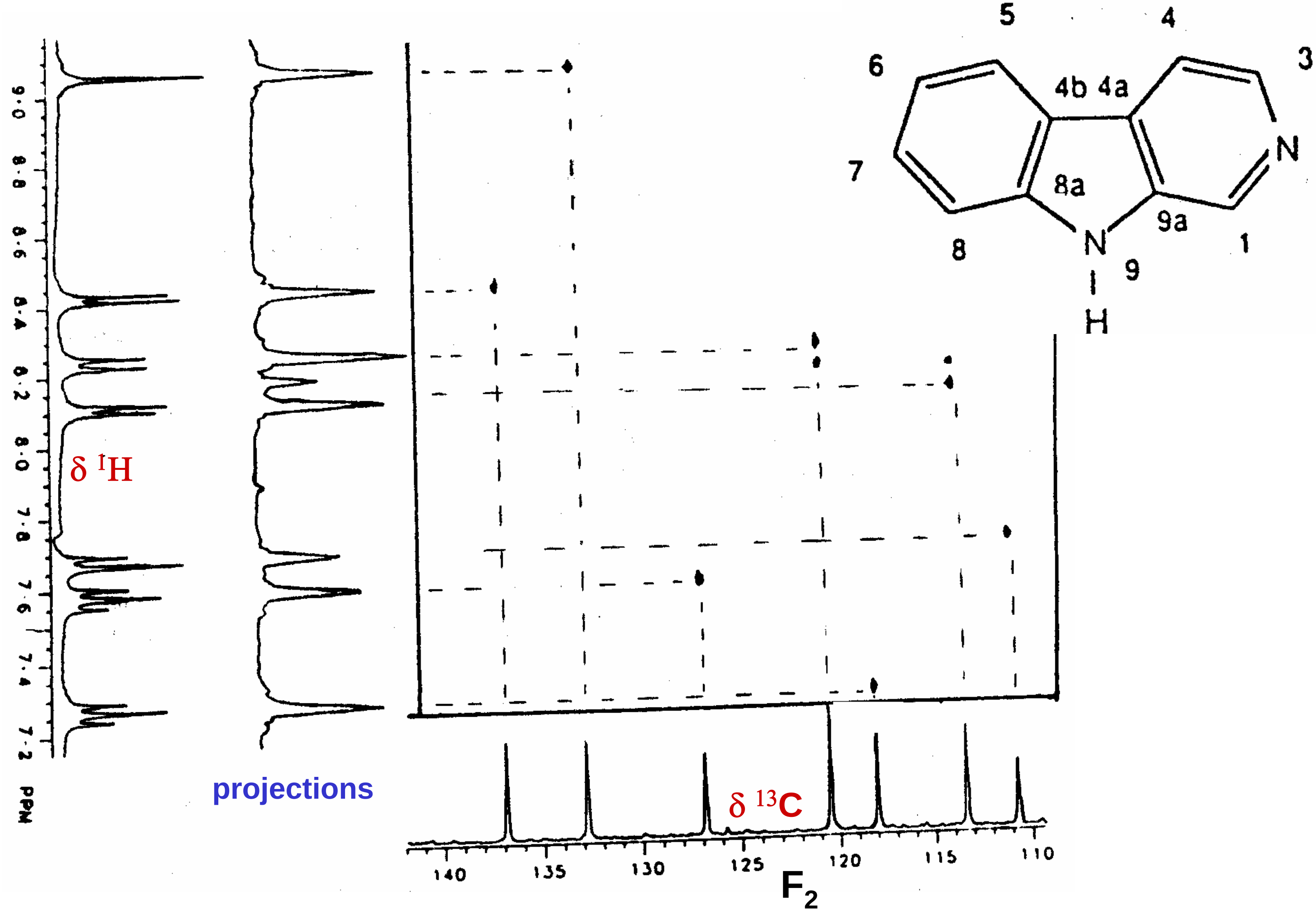
No cross peaks:
quarternary carbon,
-OH, -NH2, -X…



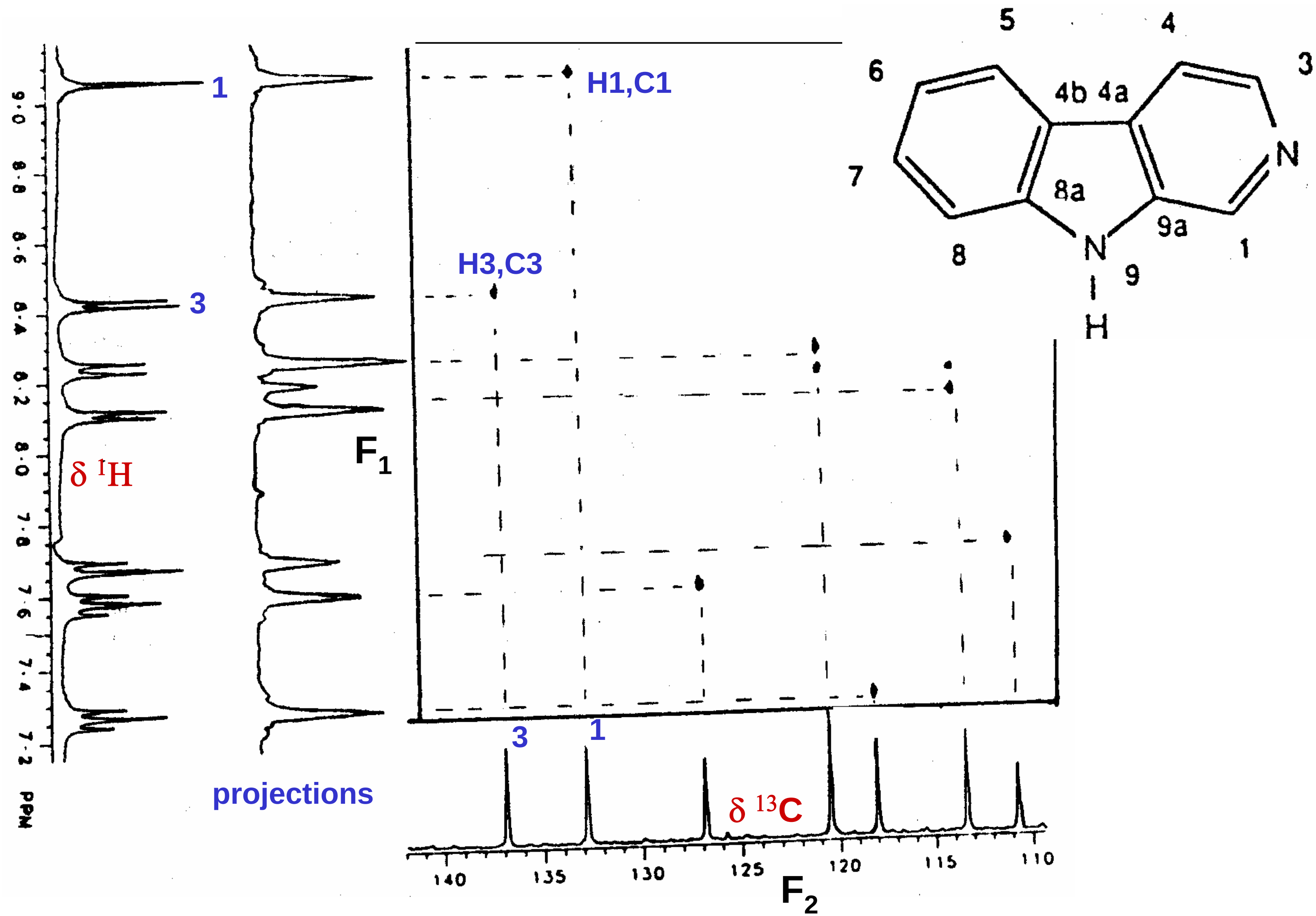


2D ^{13}C-^{1}H COSY spectrum of Norhamane

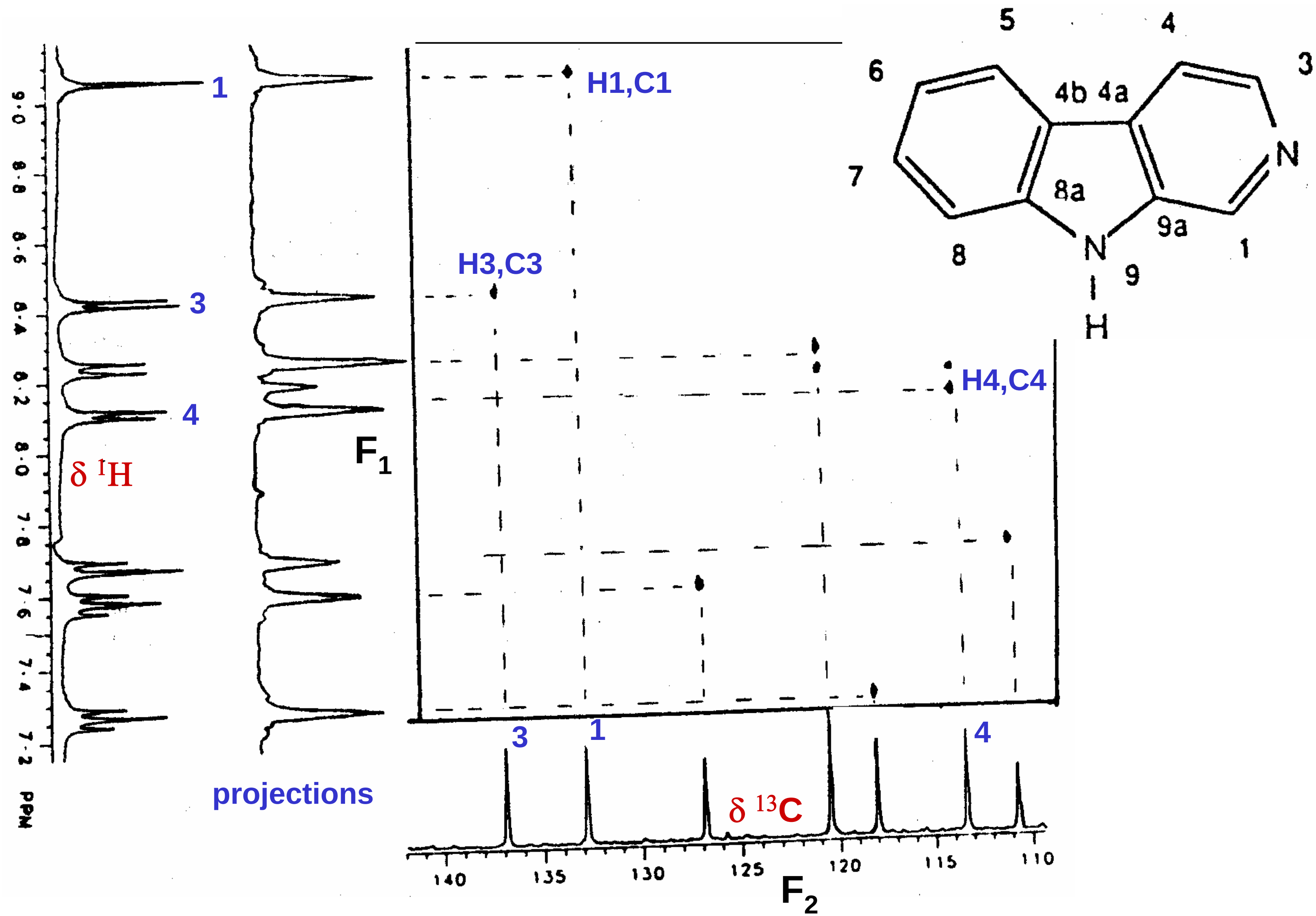
($^{1}J_{CH}$ correlations)



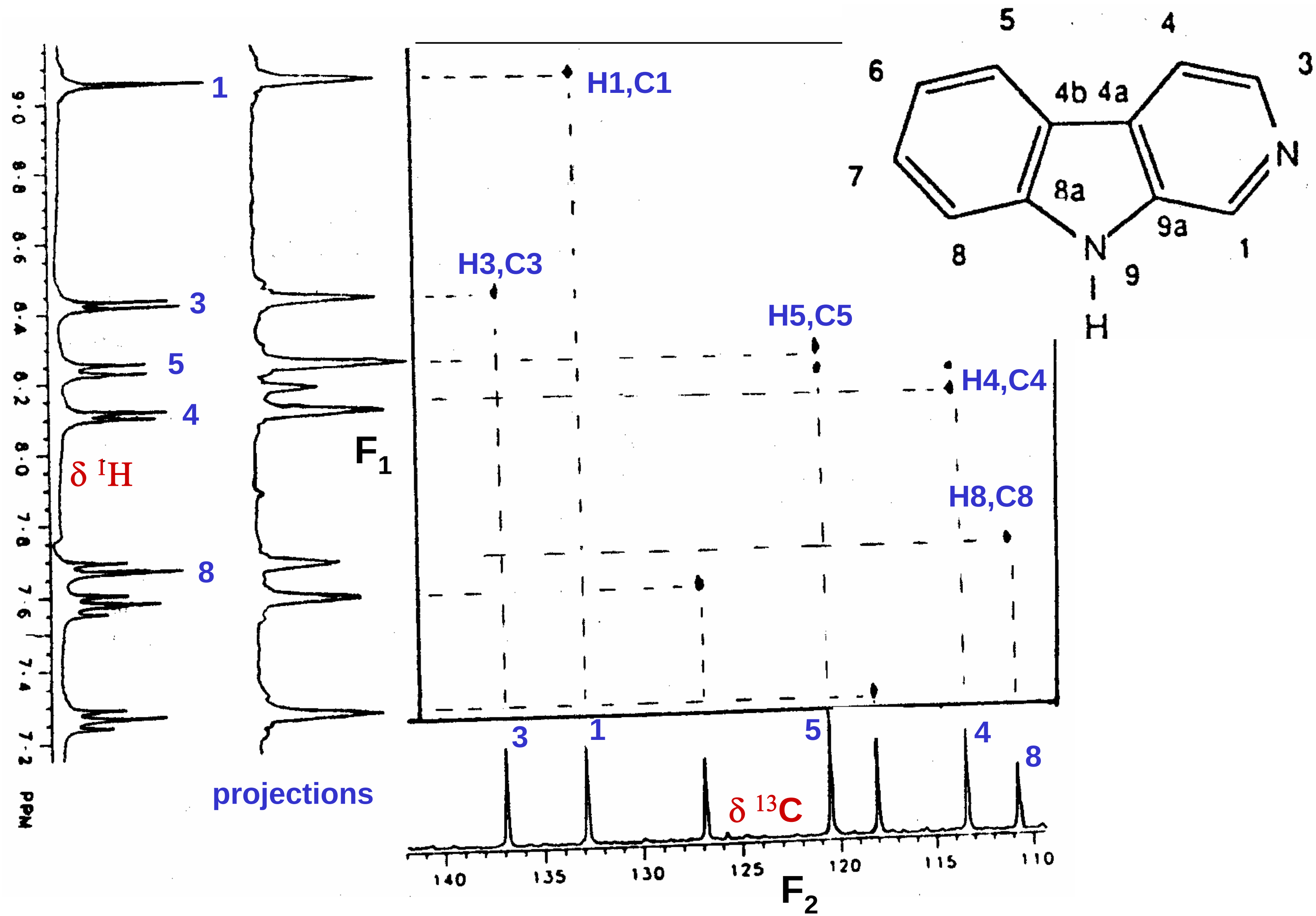
2D ^{13}C-^{1}H COSY spectrum of Norhamane
($^{1}J_{CH}$ correlations)



2D ^{13}C-^{1}H COSY spectrum of Norhamane
($^{1}J_{CH}$ correlations)

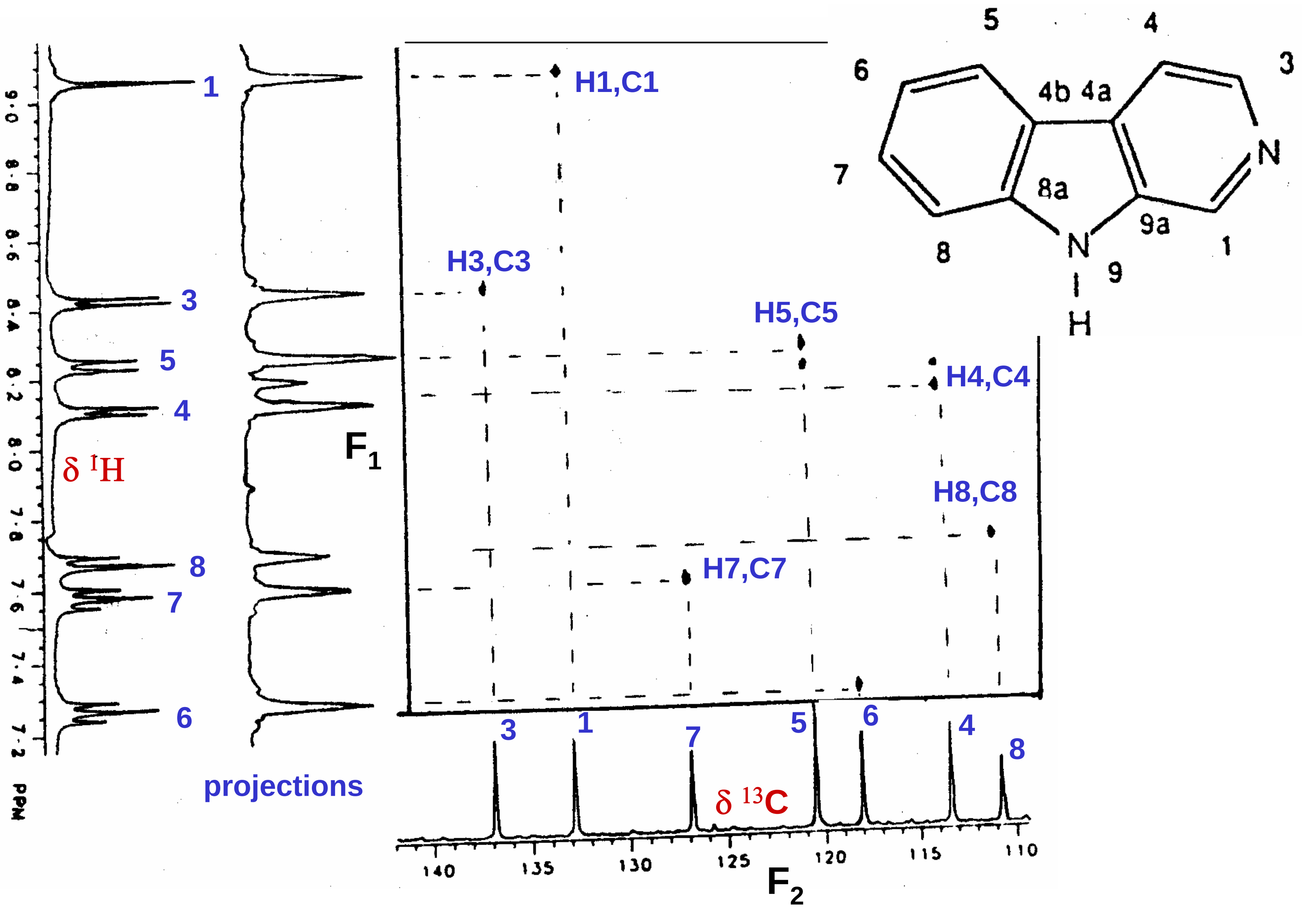


2D ^{13}C-^{1}H COSY spectrum of Norhamane
($^{1}J_{CH}$ correlations)

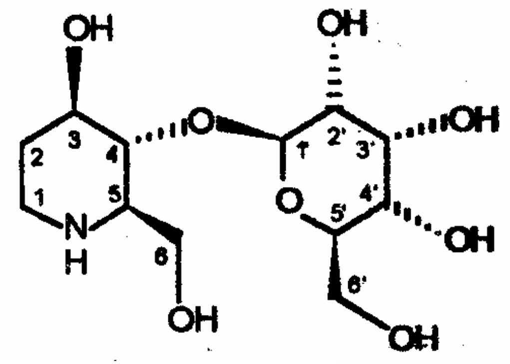


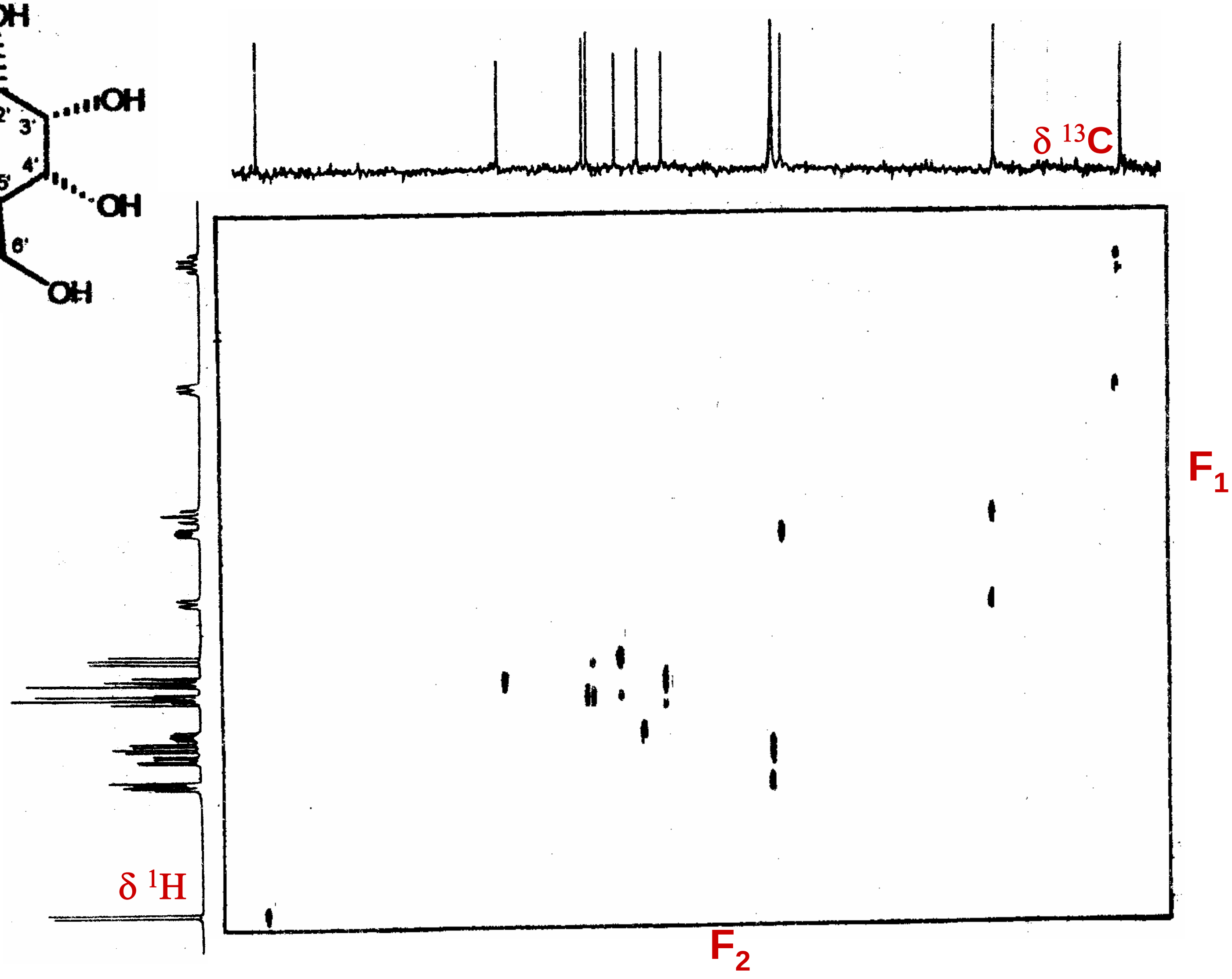
2D ^{13}C-^{1}H COSY spectrum of Norhamane

($^{1}J_{CH}$ correlations)

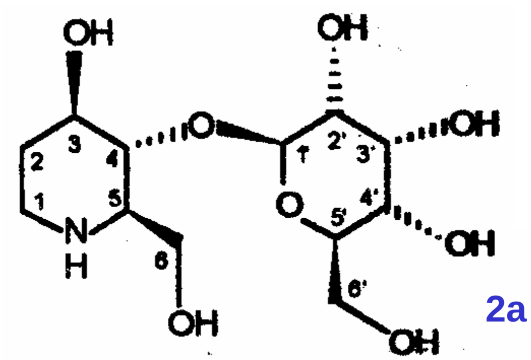


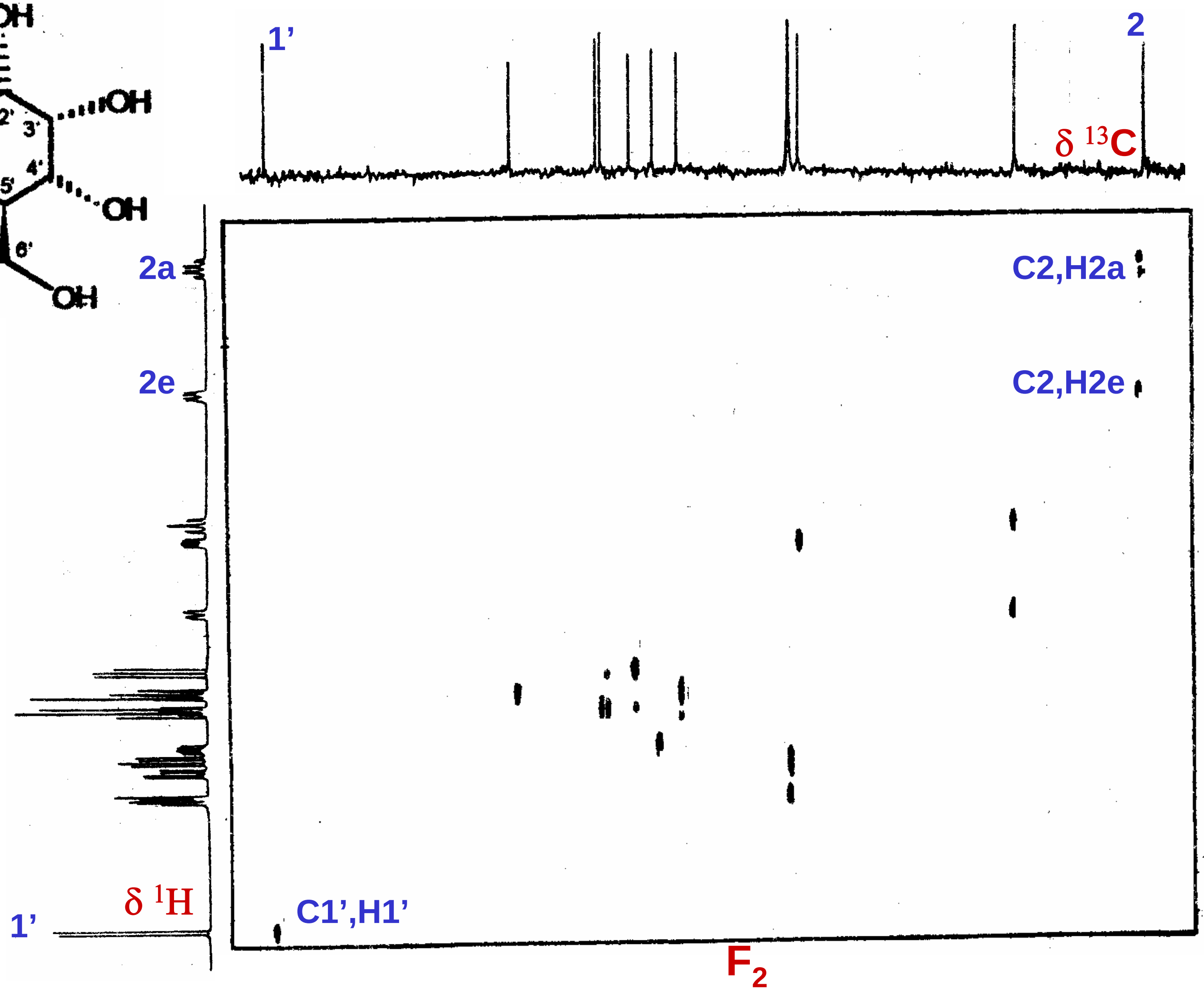
2D ^{13}C-^{1}H COSY spectrum ($^{1}J_{CH}$ correlations)



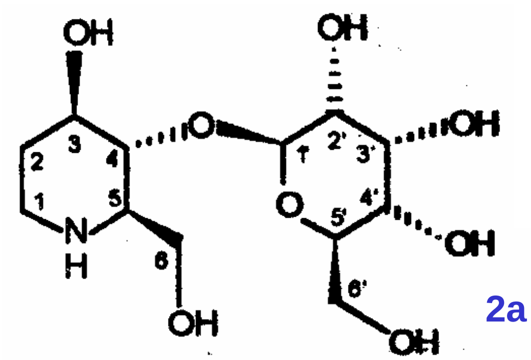


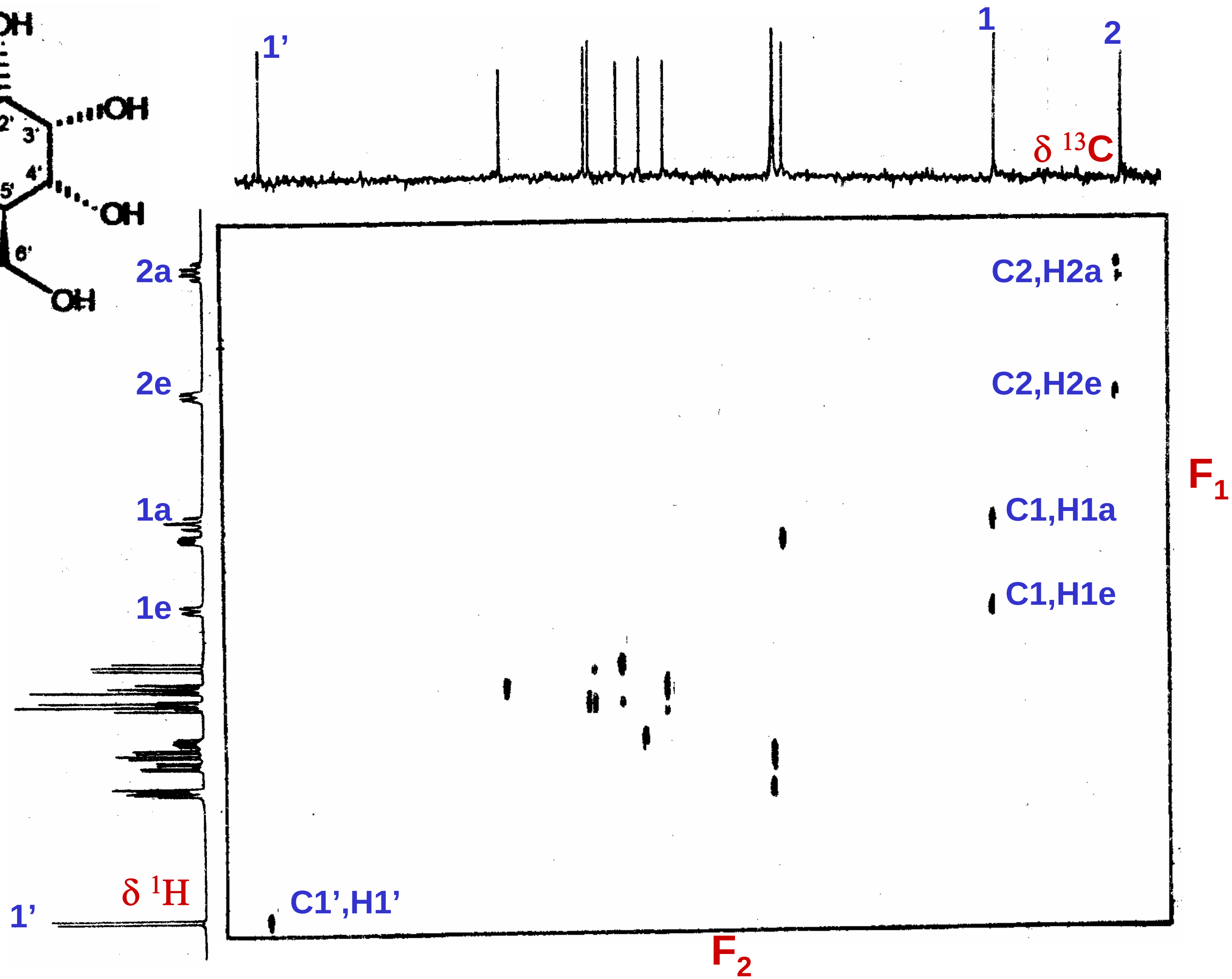
2D ^{13}C-^{1}H COSY spectrum ($^{1}J_{CH}$ correlations)



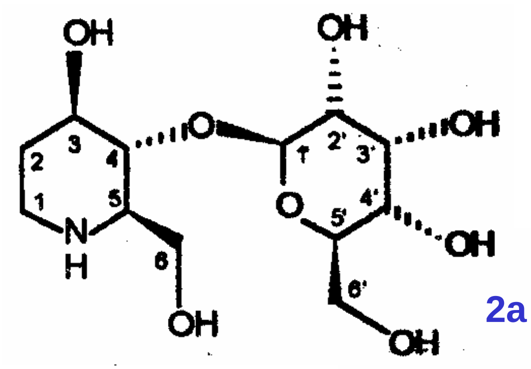


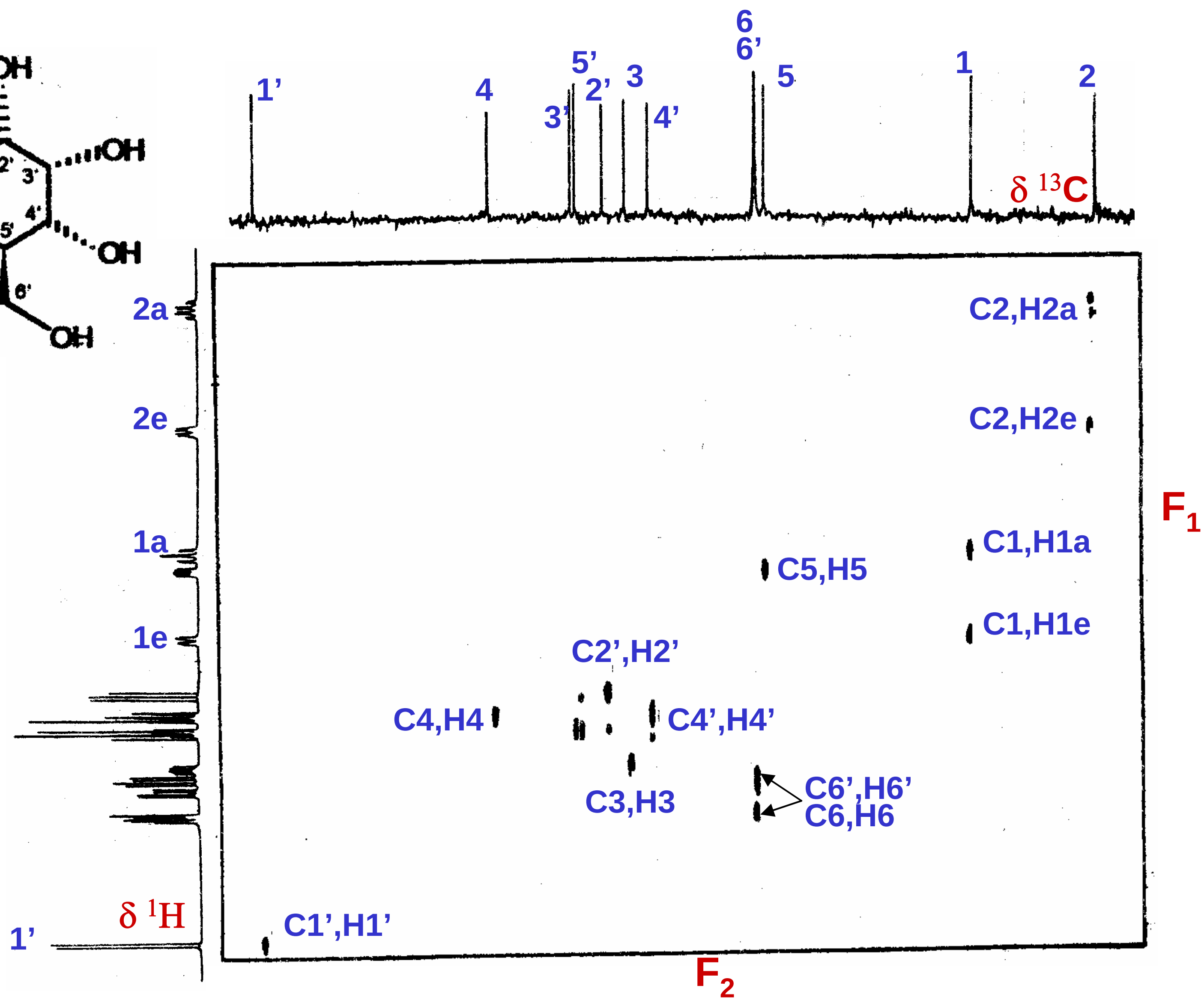
2D ^{13}C-^{1}H COSY spectrum ($^{1}J_{CH}$ correlations)





2D ^{13}C-^{1}H COSY spectrum ($^{1}J_{CH}$ correlations)



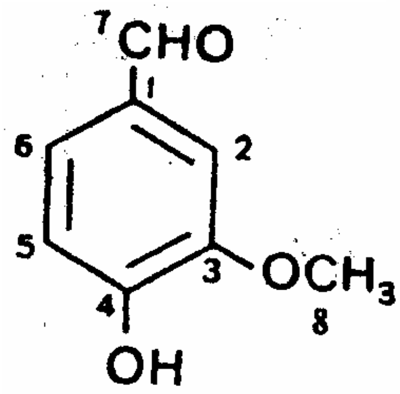


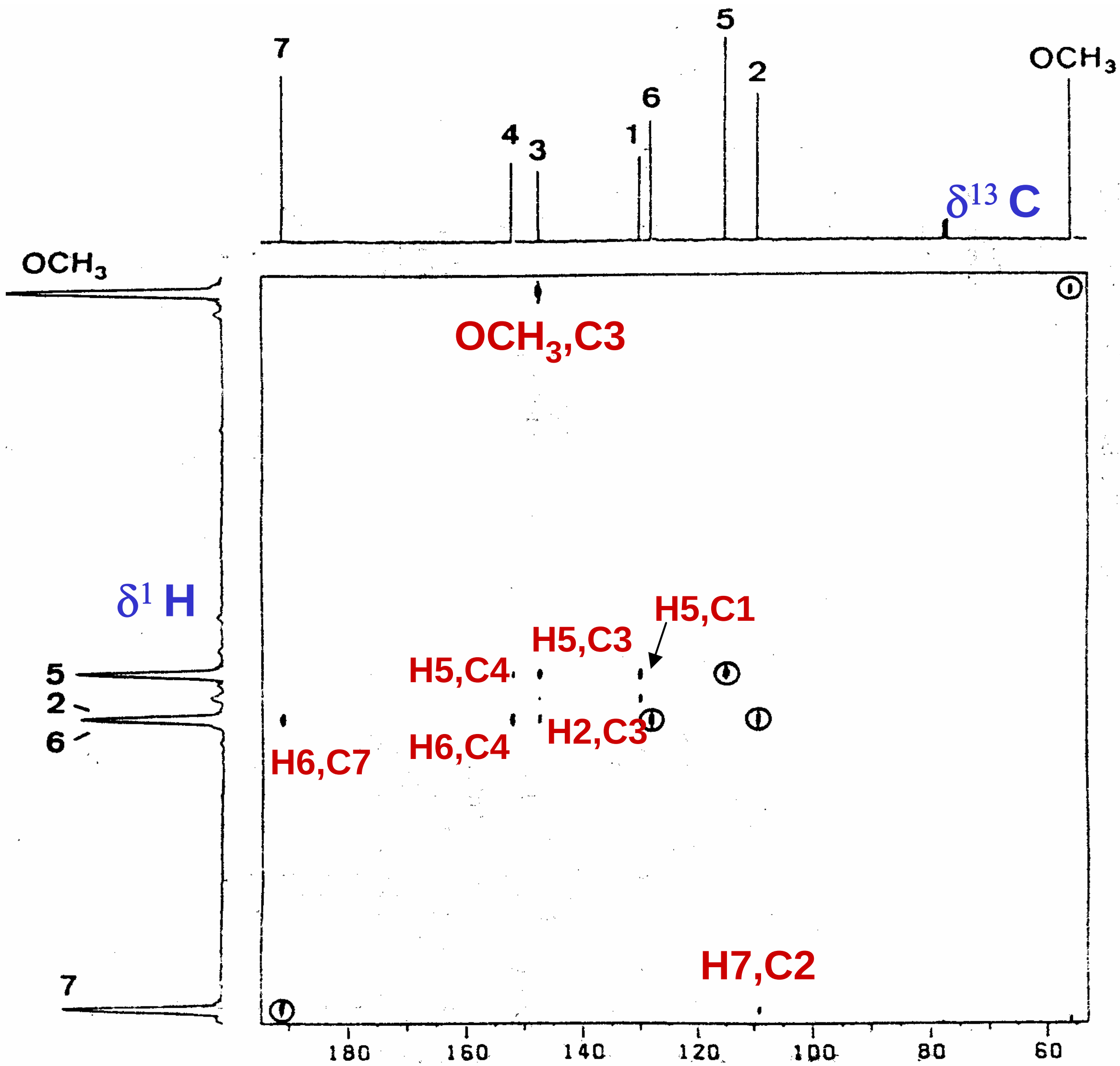
Detection of Long-Range Connectivities

Optimized Heteronuclear Polarization Transfer via Long-Range J

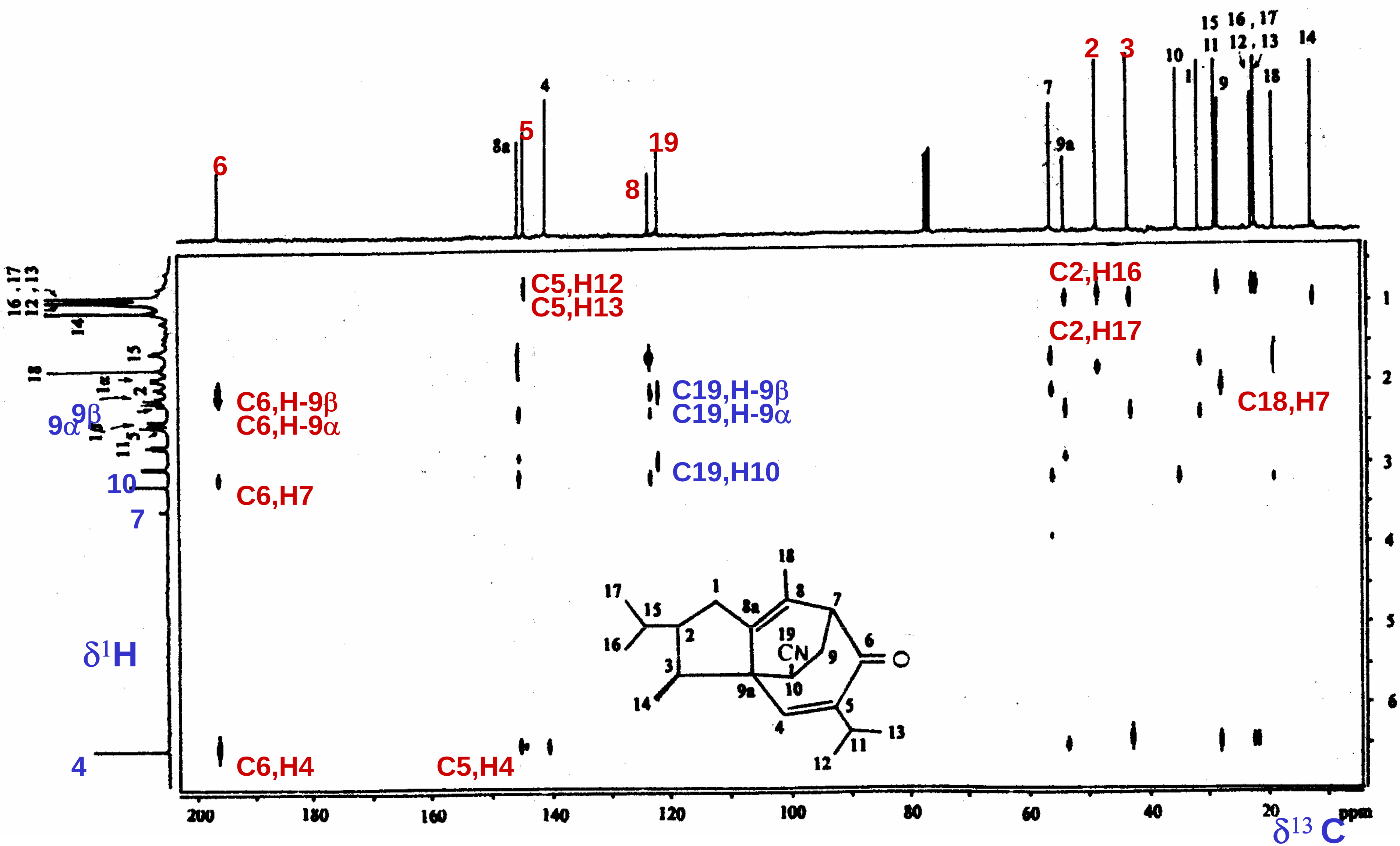
COLOC (Correlation LOng- range Couplings) spectrum

($^{n}J_{CH}$ correlations)

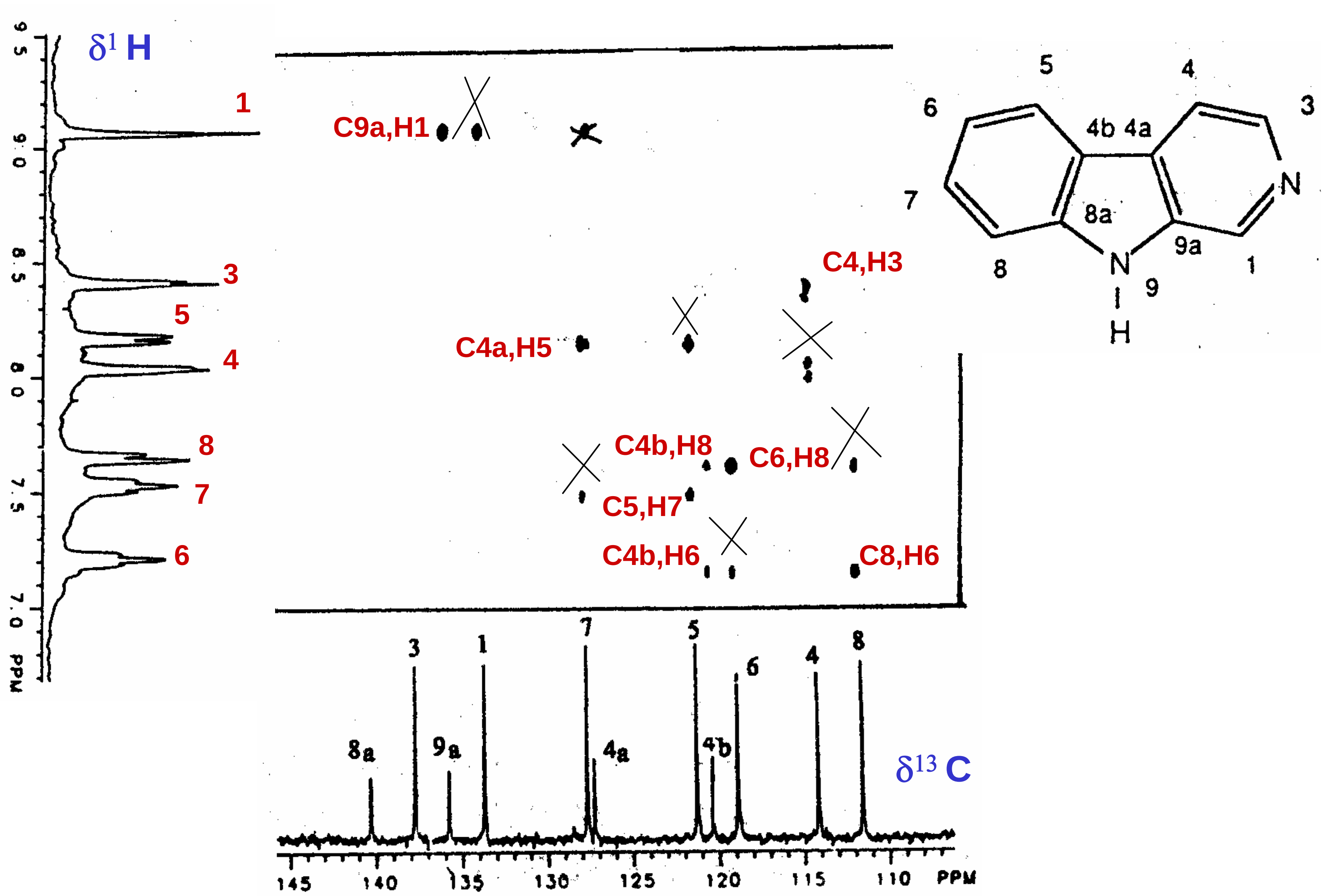




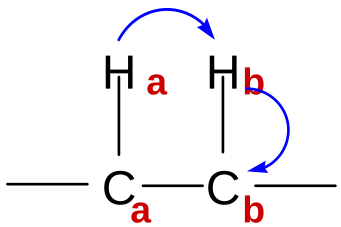
2D COLOC Spectrum



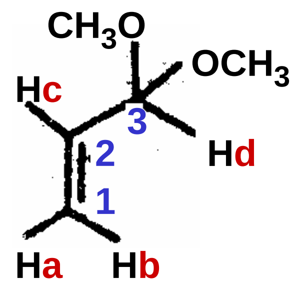
2D COLOC Spectrum of Norharmane

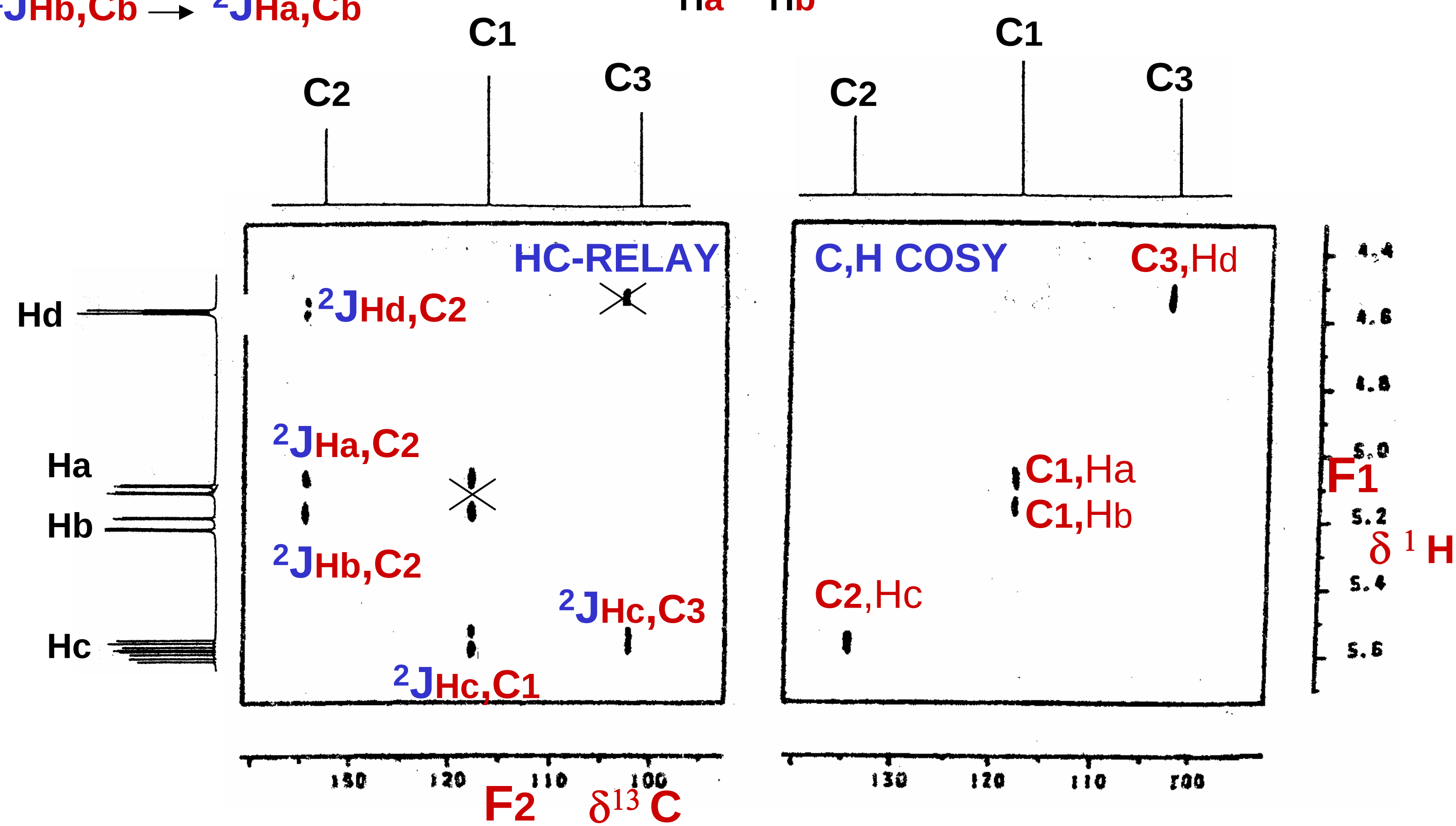


Heteronuclear Relayed Coherence Transfer
2D H-H-C Relay Spectrum

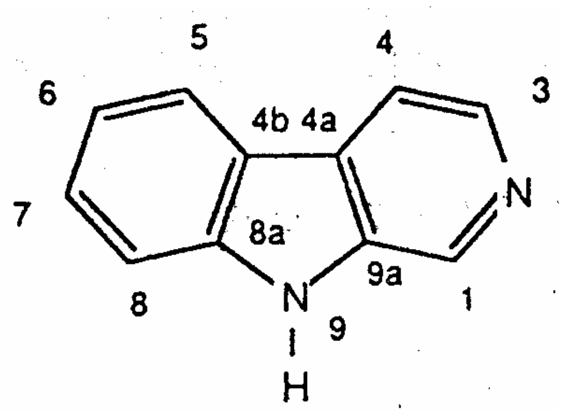


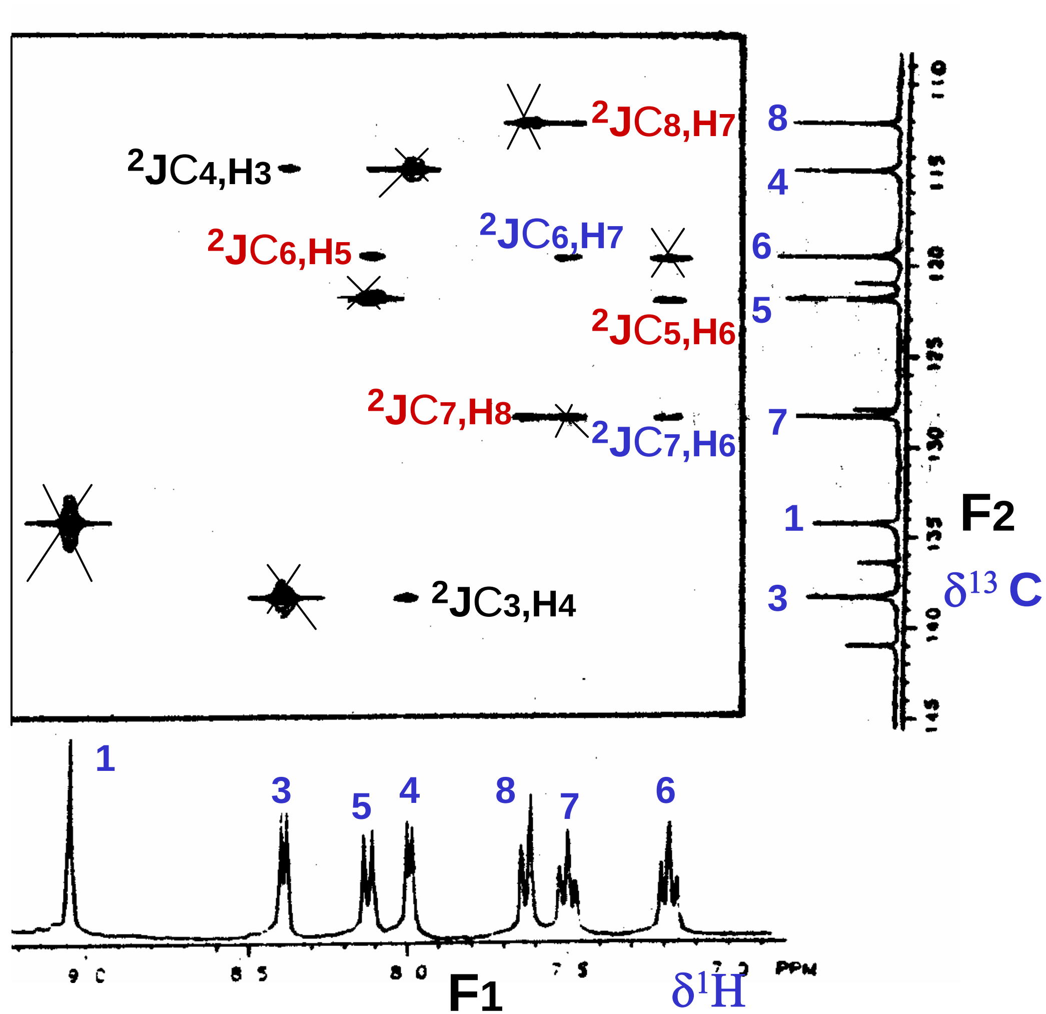
$^{3}J_{Ha,Hb}$ → $^{1}J_{Hb,Cb}$ → $^{2}J_{Ha,Cb}$



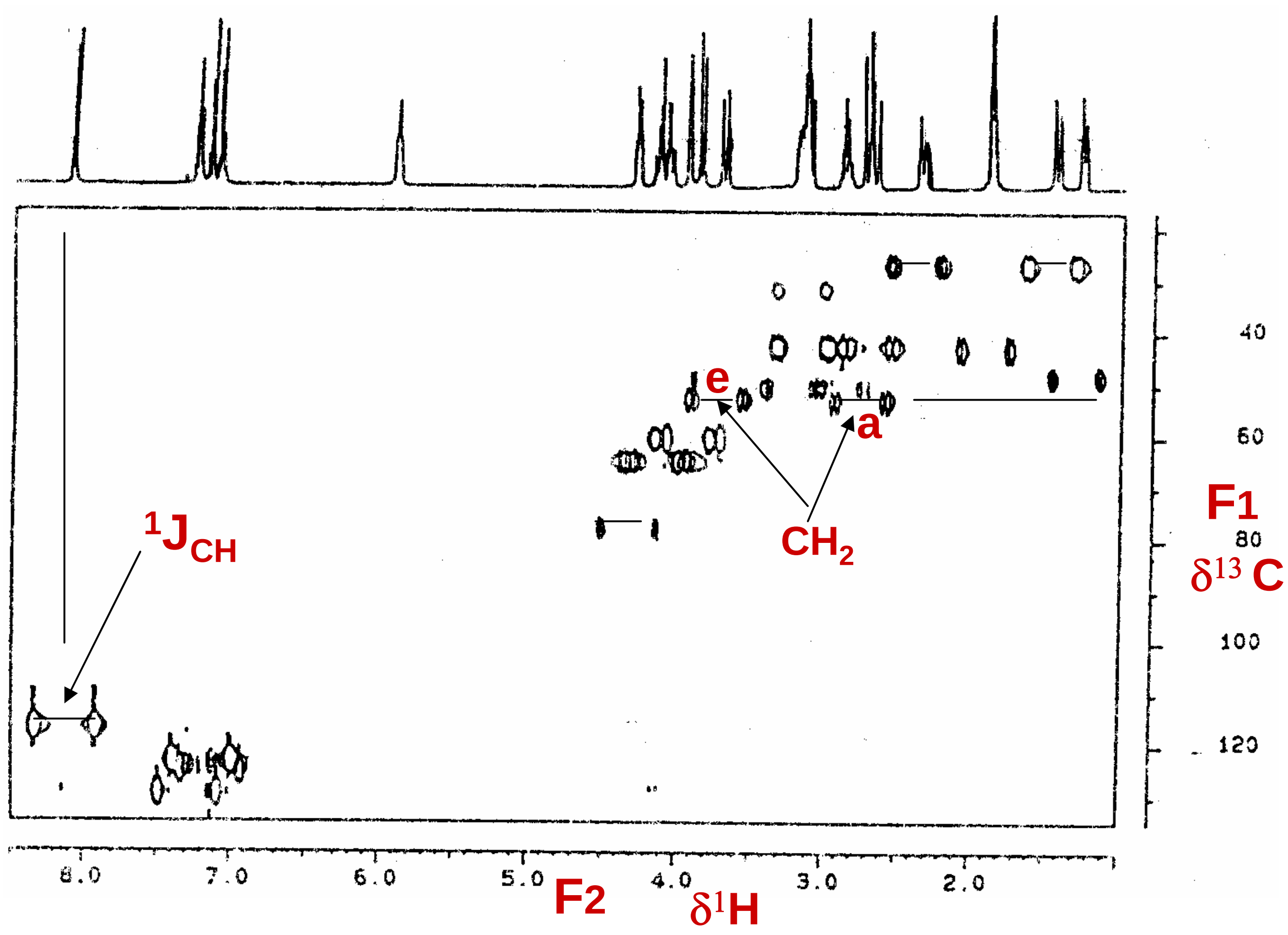


2D H-H-C Relay Spectrum of Norharmane

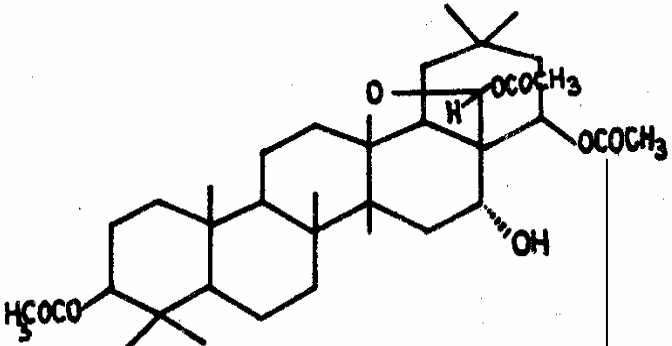


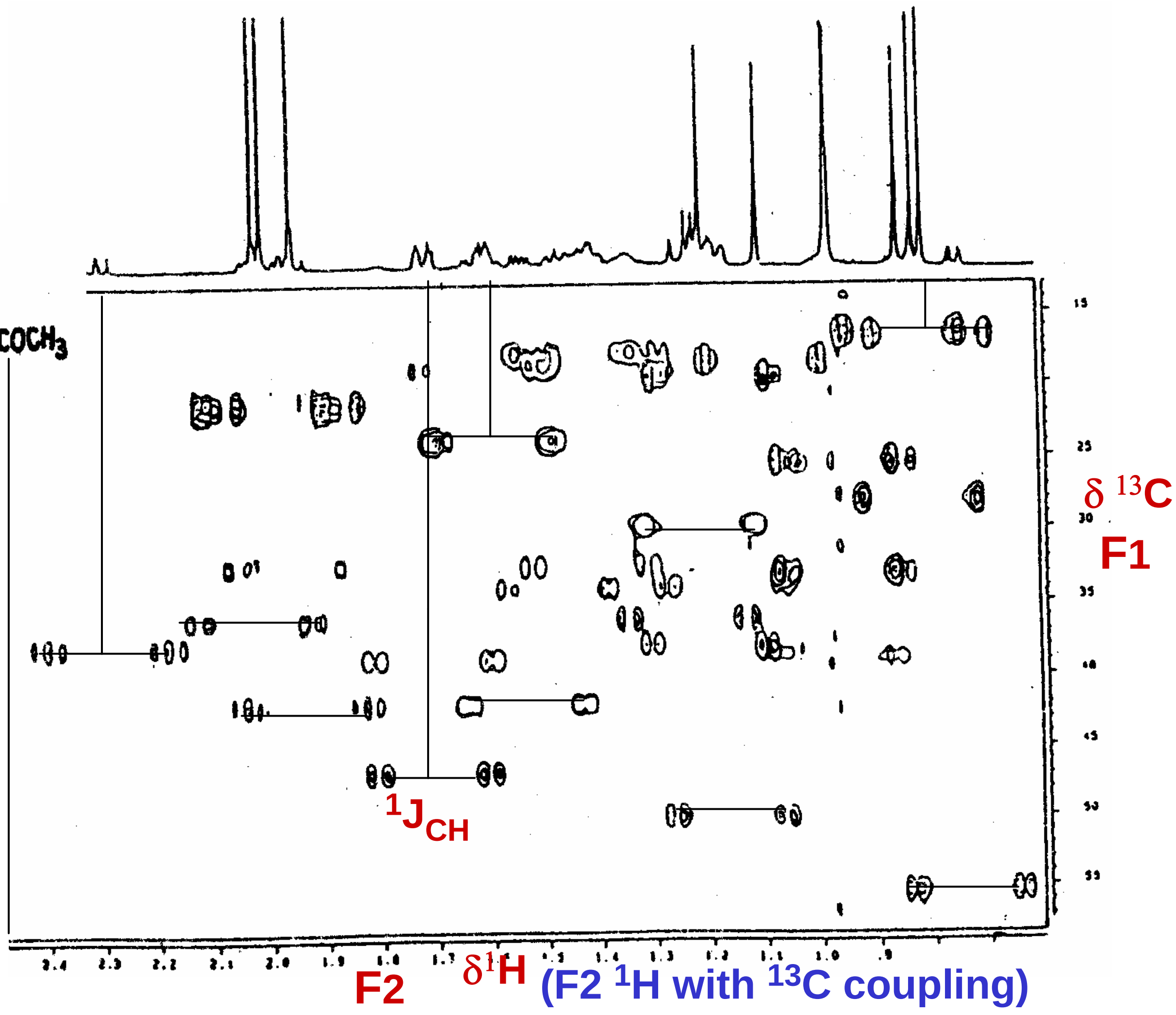


Proton- Detected HETCOR: HMQC Inverse Experiments
(Heteronuclear Multiple Quantum Coherence) $^{1}J_{CH}$



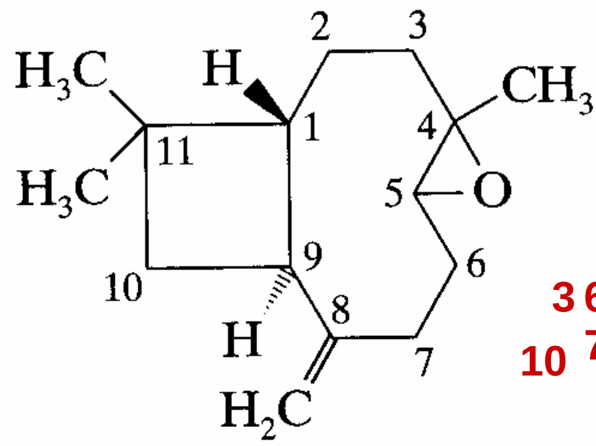
HMQC Inverse Experiment spectrum ($^{1}J_{CH}$)

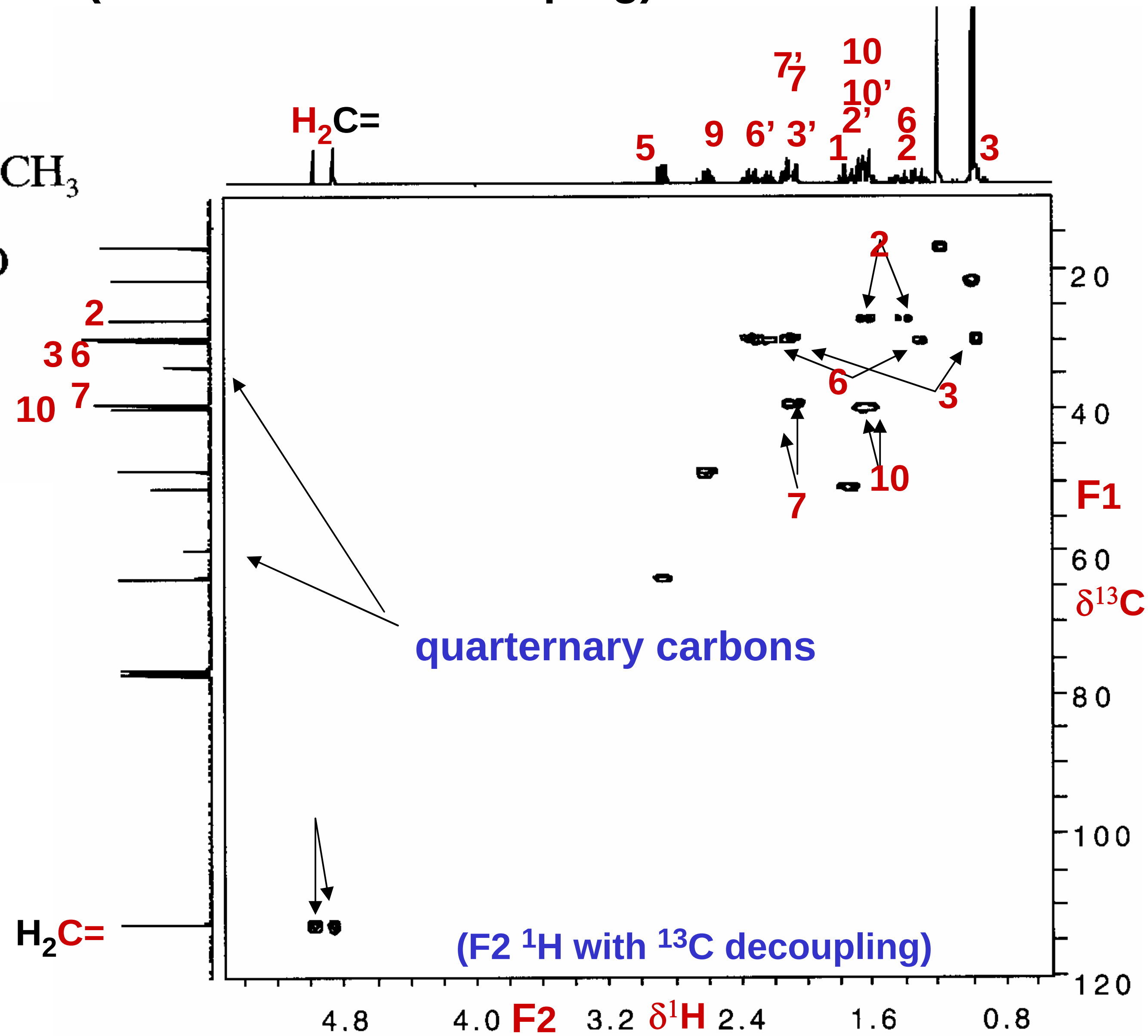




HMQC spectrum of caryophyllene oxide

(F2 ^{1}H with ^{13}C decouplng)



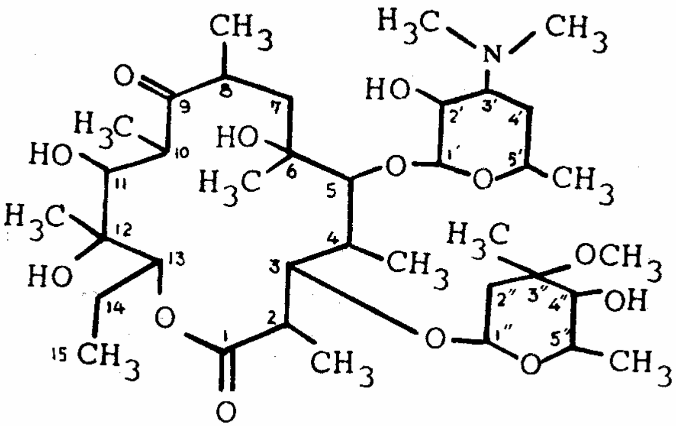


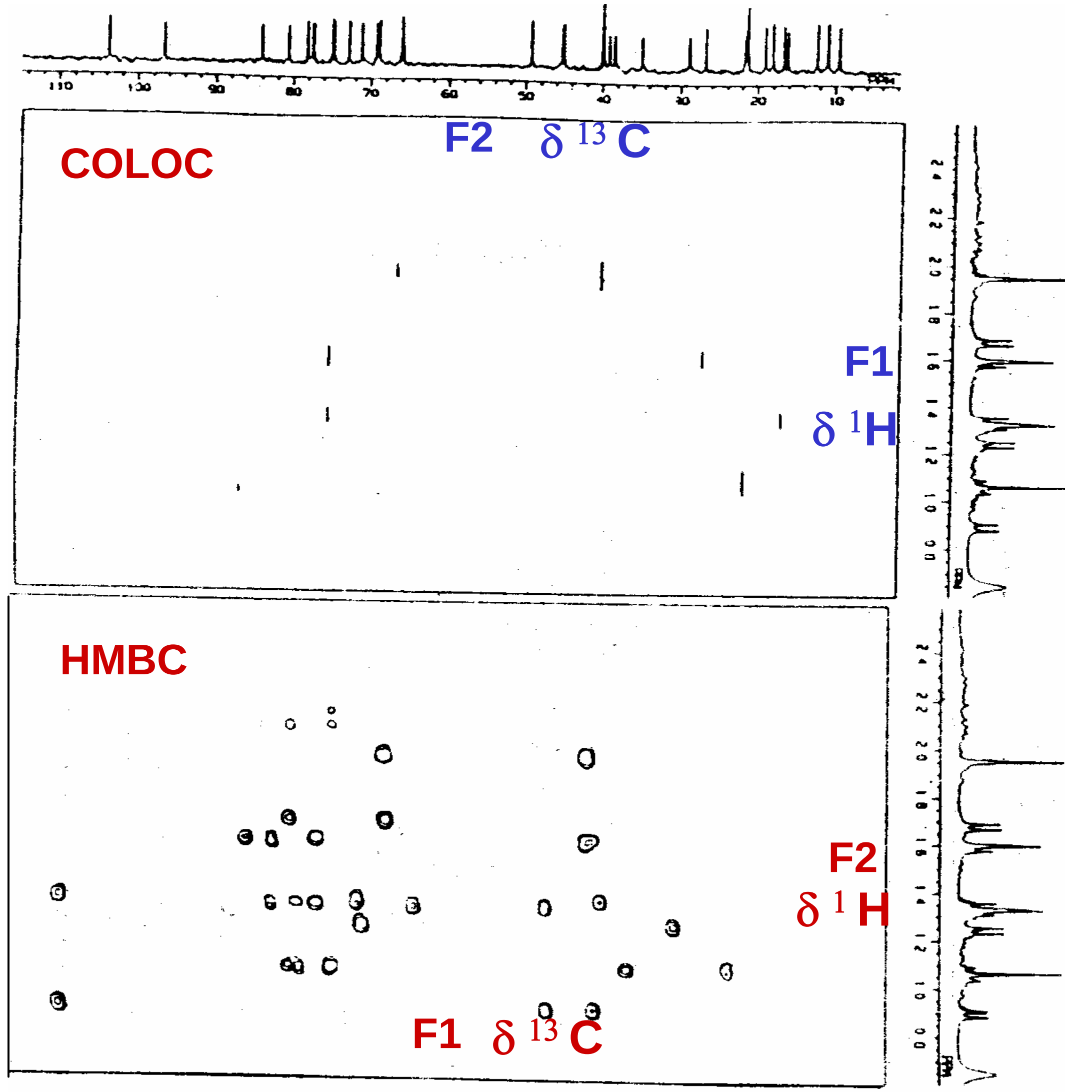
Proton- Detected Long- range ^{1}H-^{13}C Heteronuclear Correlation:

HMBC Inverse Experiment ($^{n}J_{CH}$)

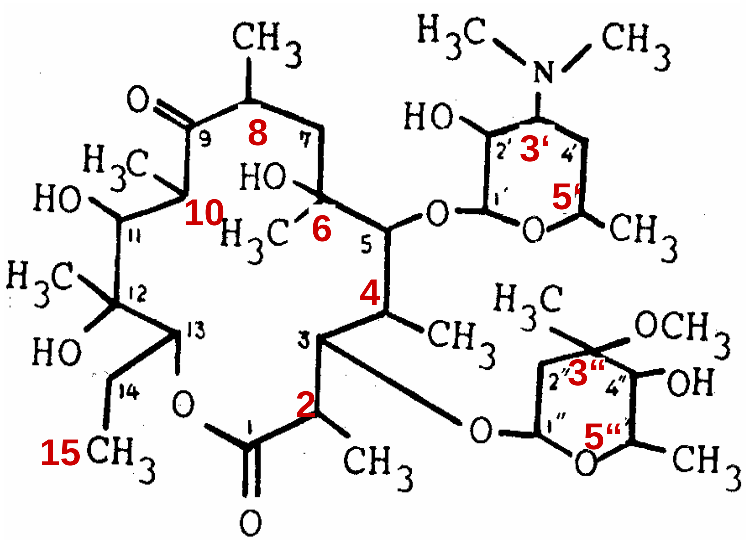
(Heteronuclear Multiple Bond Coherence)

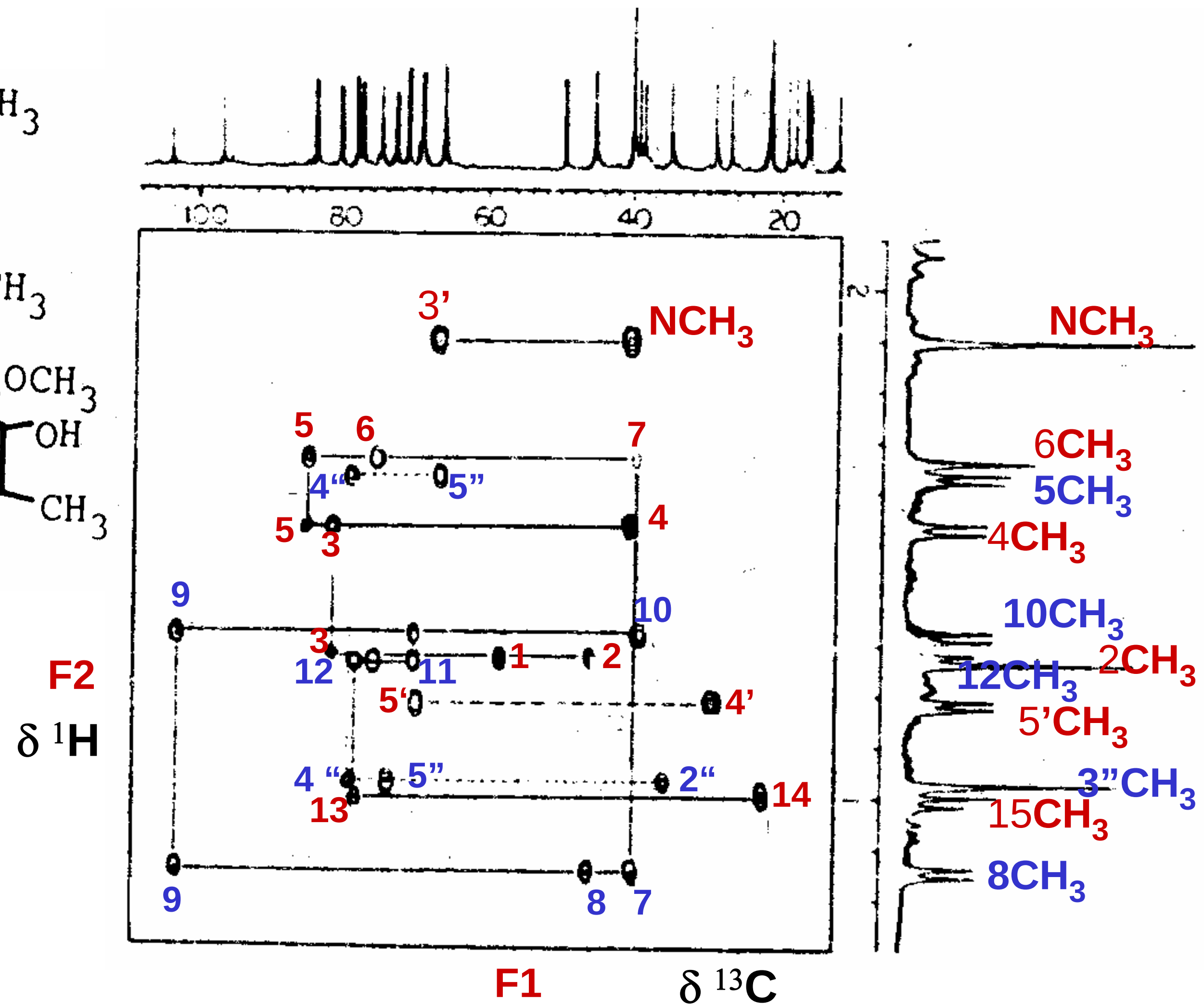
Comparison of COLOC & HMBC of Sermycin



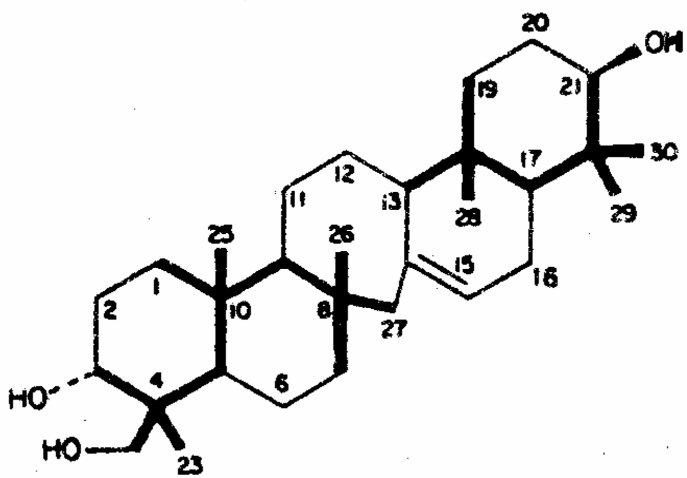


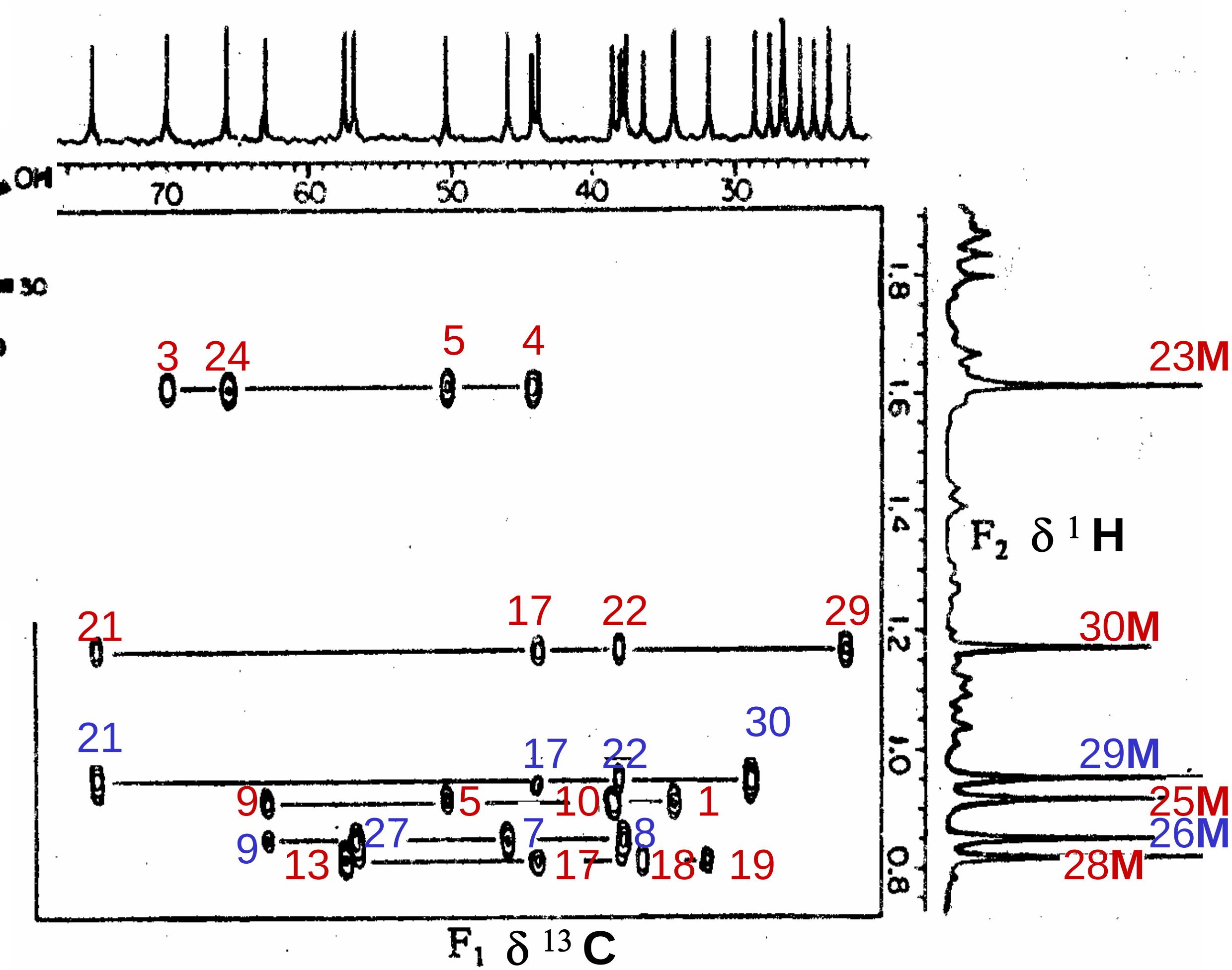
HMBC Inverse Experiment spectrum of Sermycin



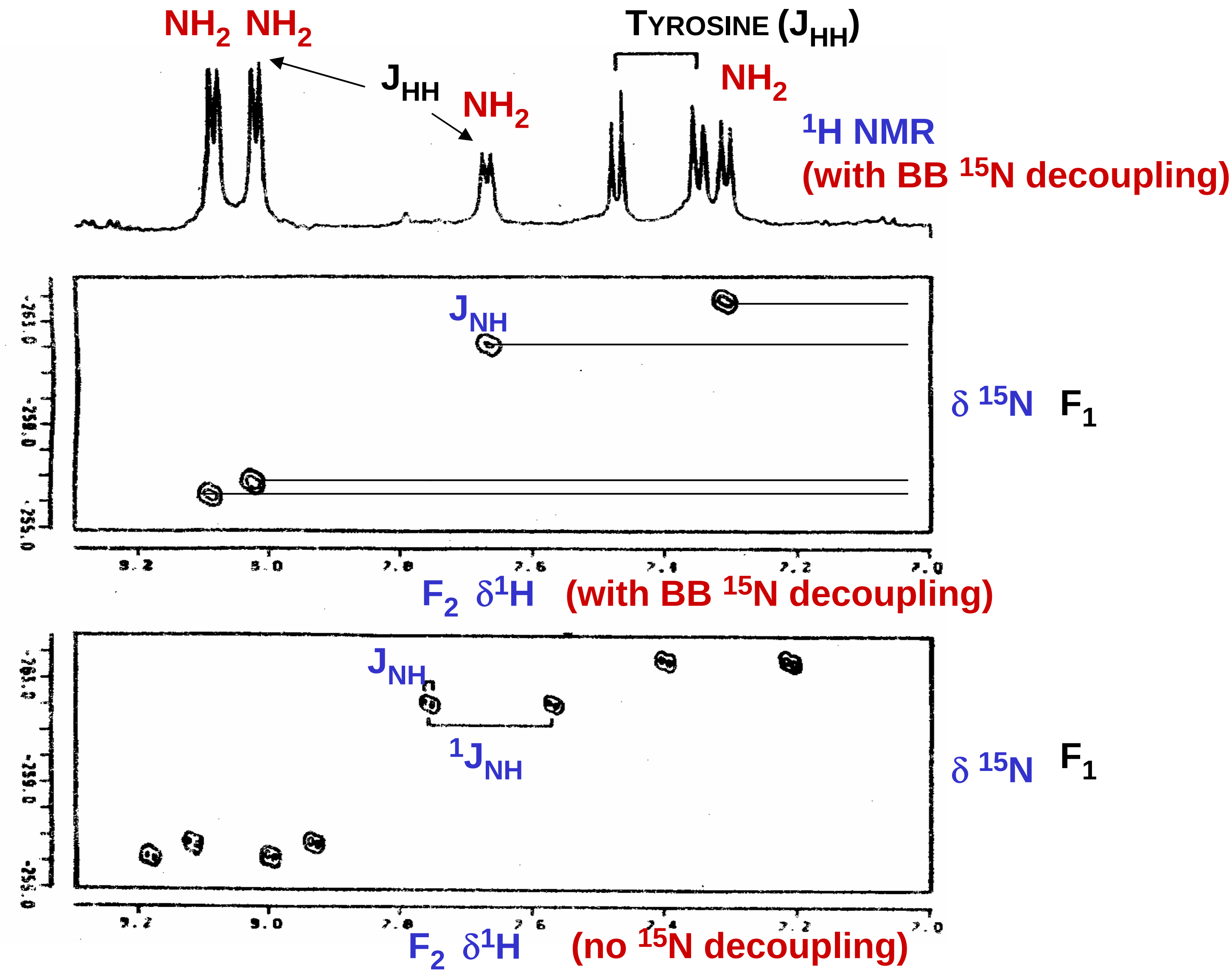


HMBC Inverse Experiment spectrum of Lycoclavannol





^{15}N-^{1}H HMBC inverse experiment spectrum of Actinomycin

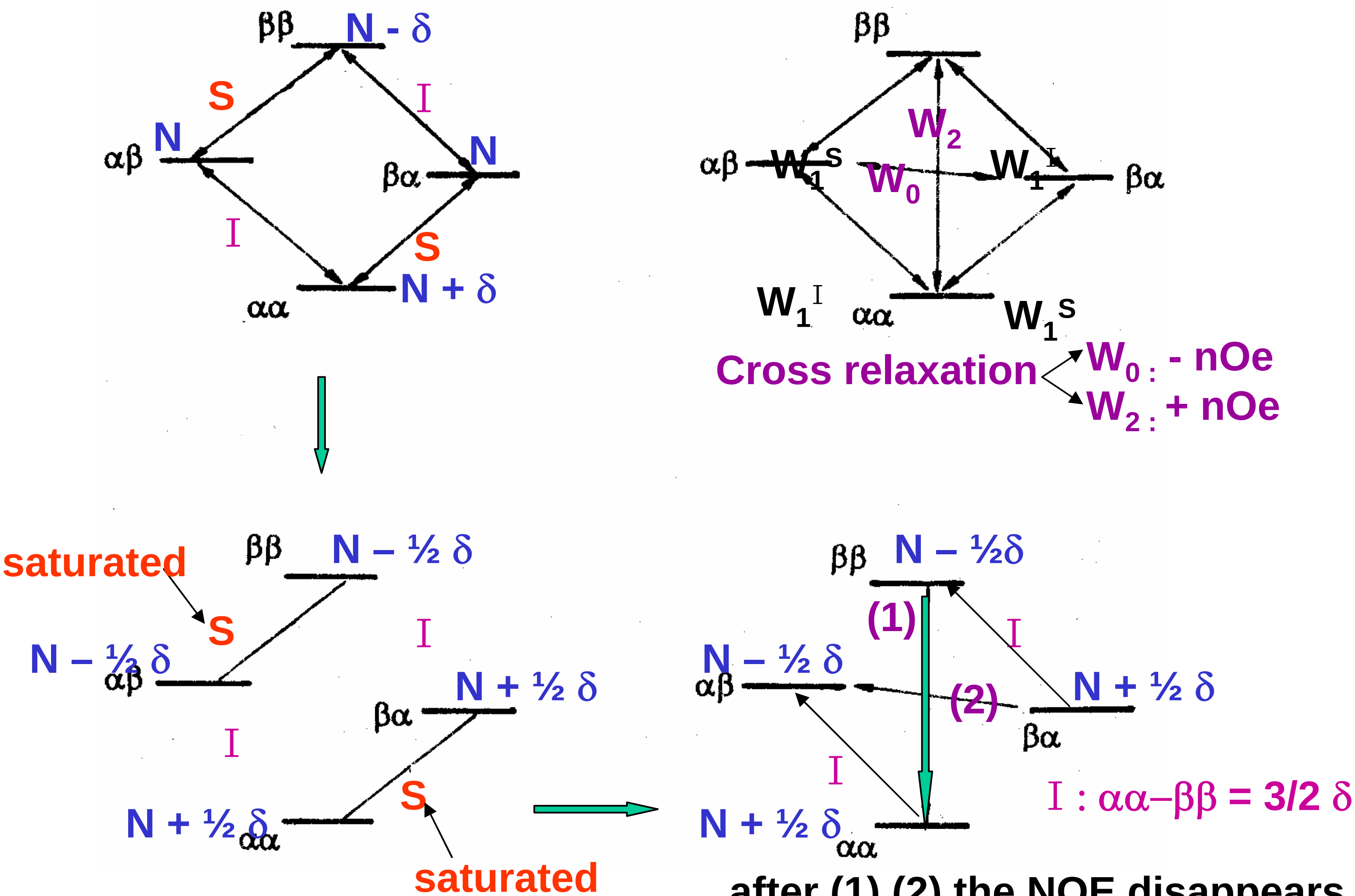


Chapter 10

Nuclear Overhauser Effect (NOE)

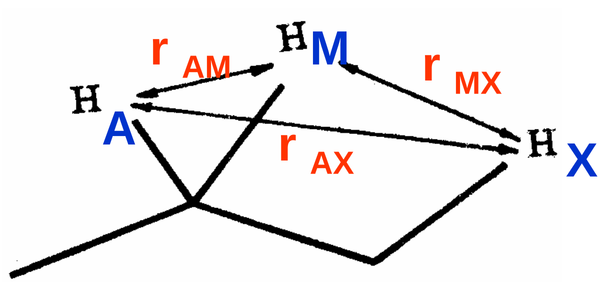
^1H-^1H Proximity Through Space

Nuclear Overhauser Effect

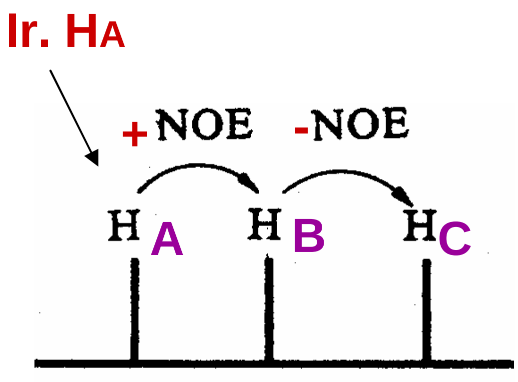


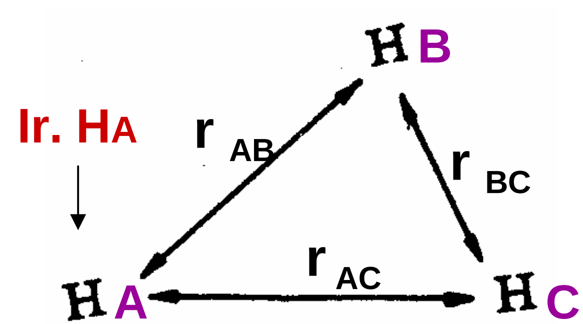
after (1),(2) the NOE disappears

Nuclear Overhauser Effect
Internuclear distances in a three-spin system



Internuclear distances in a three-spin system





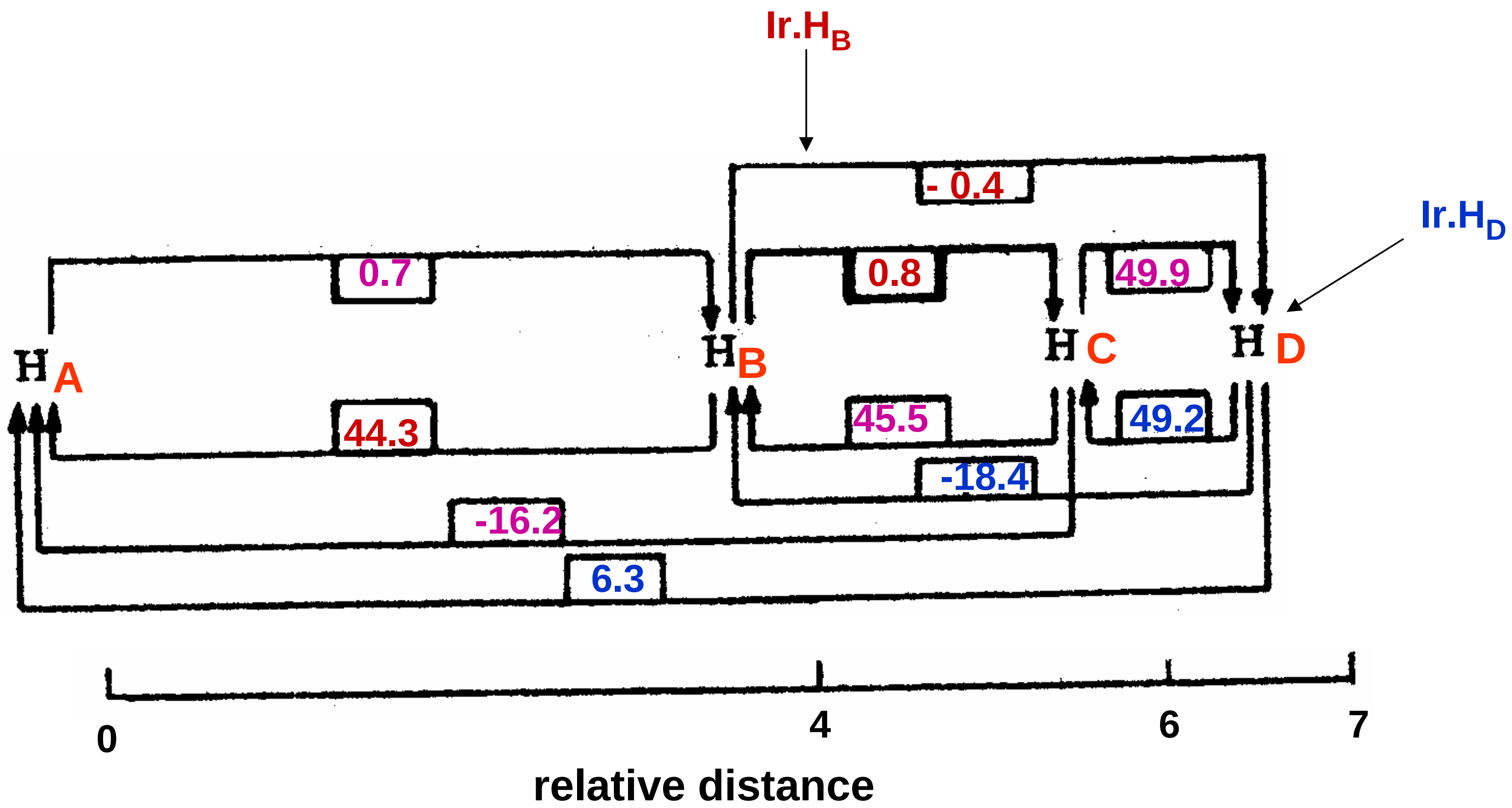
$r_{AB} = r_{AC}$:

NOE (H_C) = 0

two different arrangements in a three-spin system

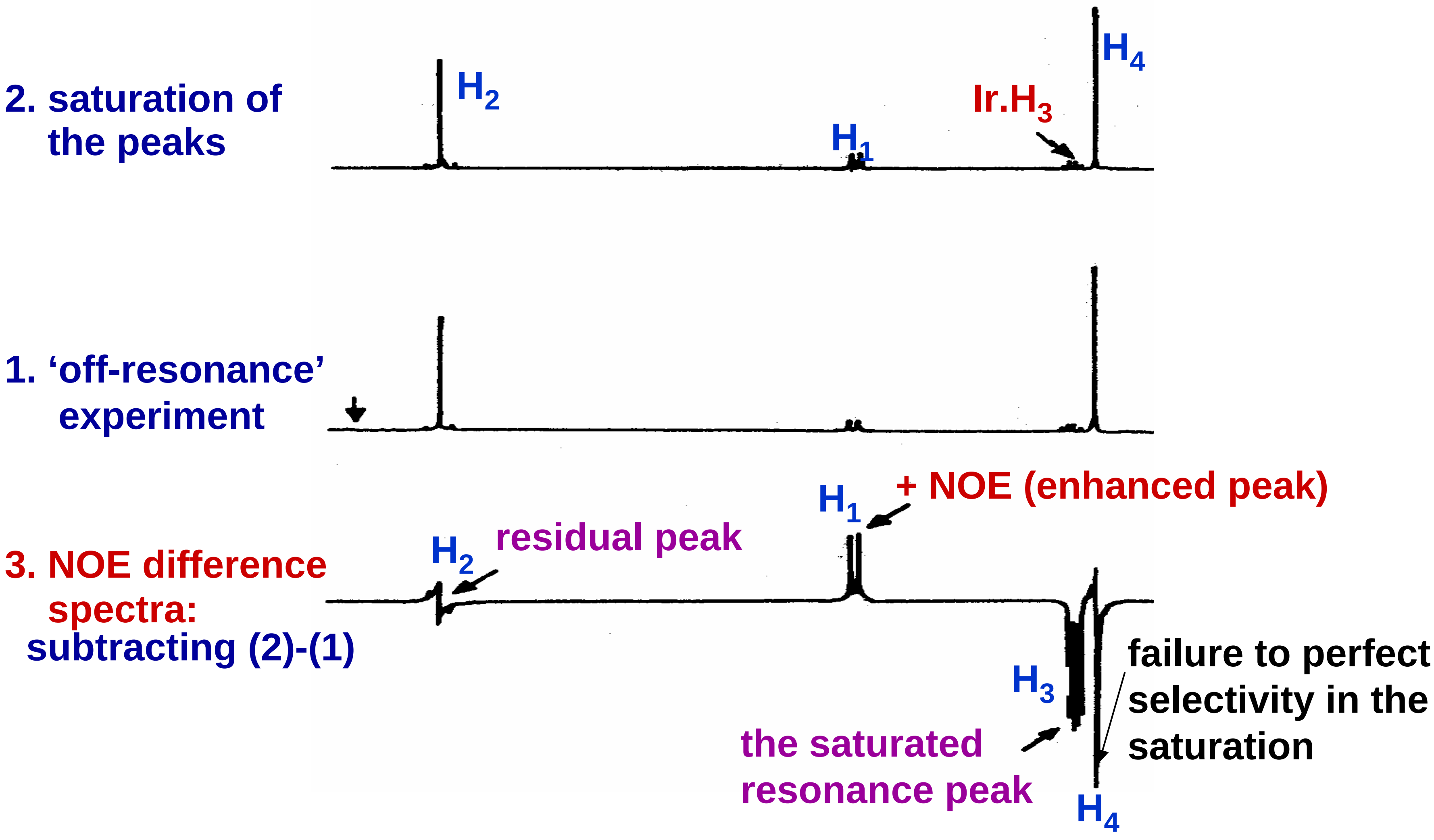
Nuclear Overhauser Effect

NOE's in a linear four-spin system

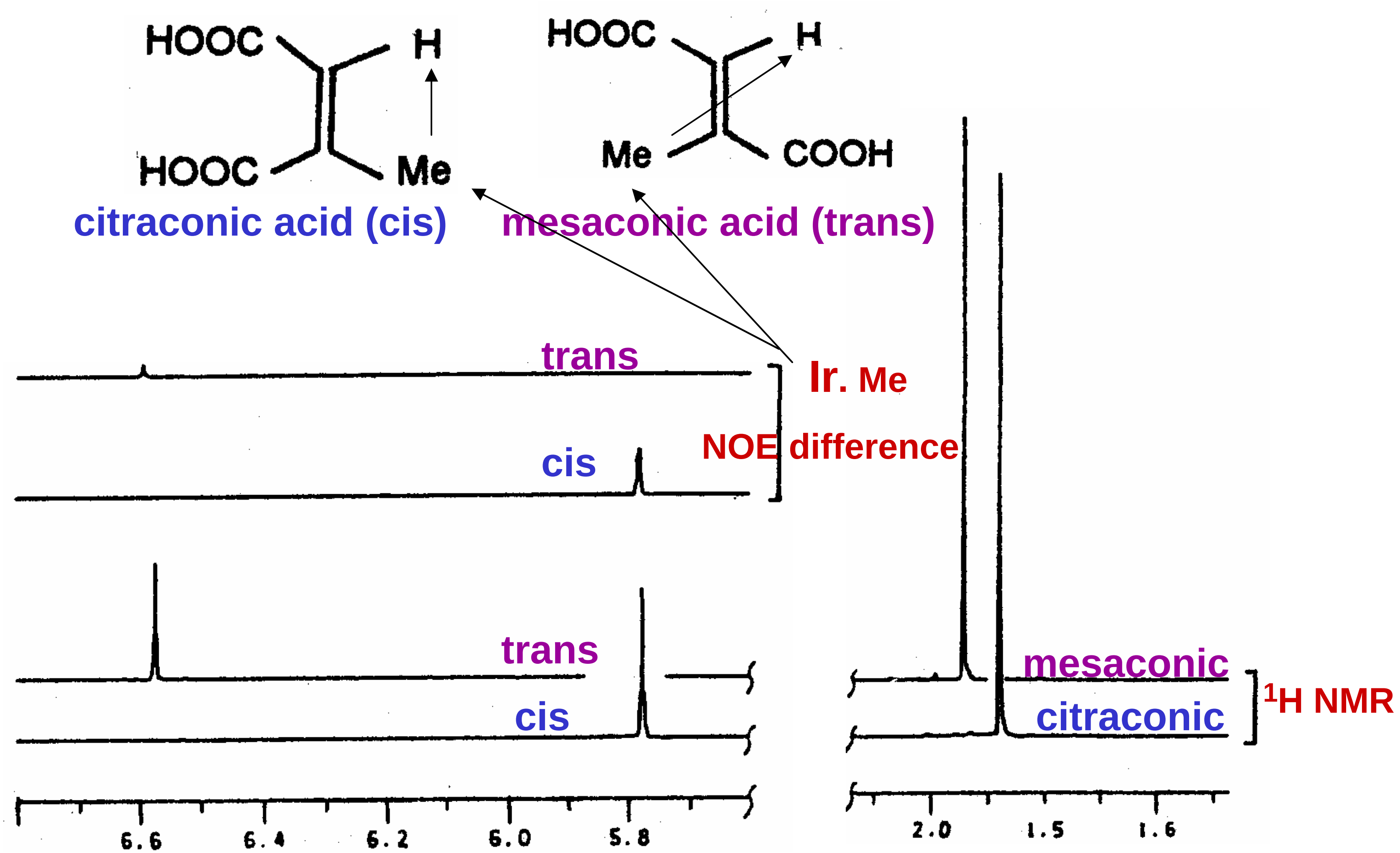


NOE measurement

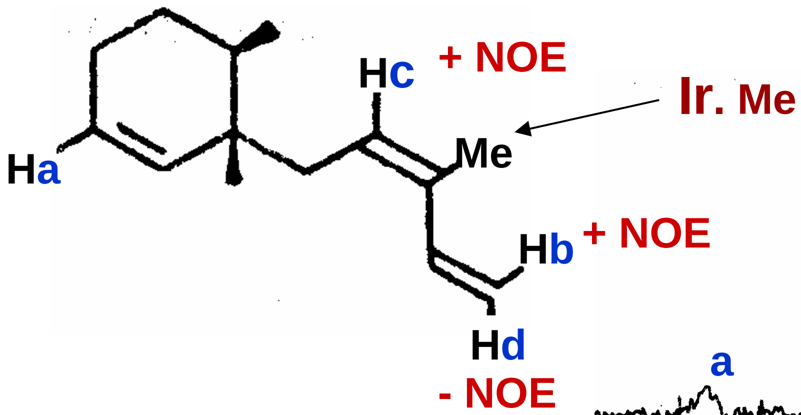
NOE difference experiments

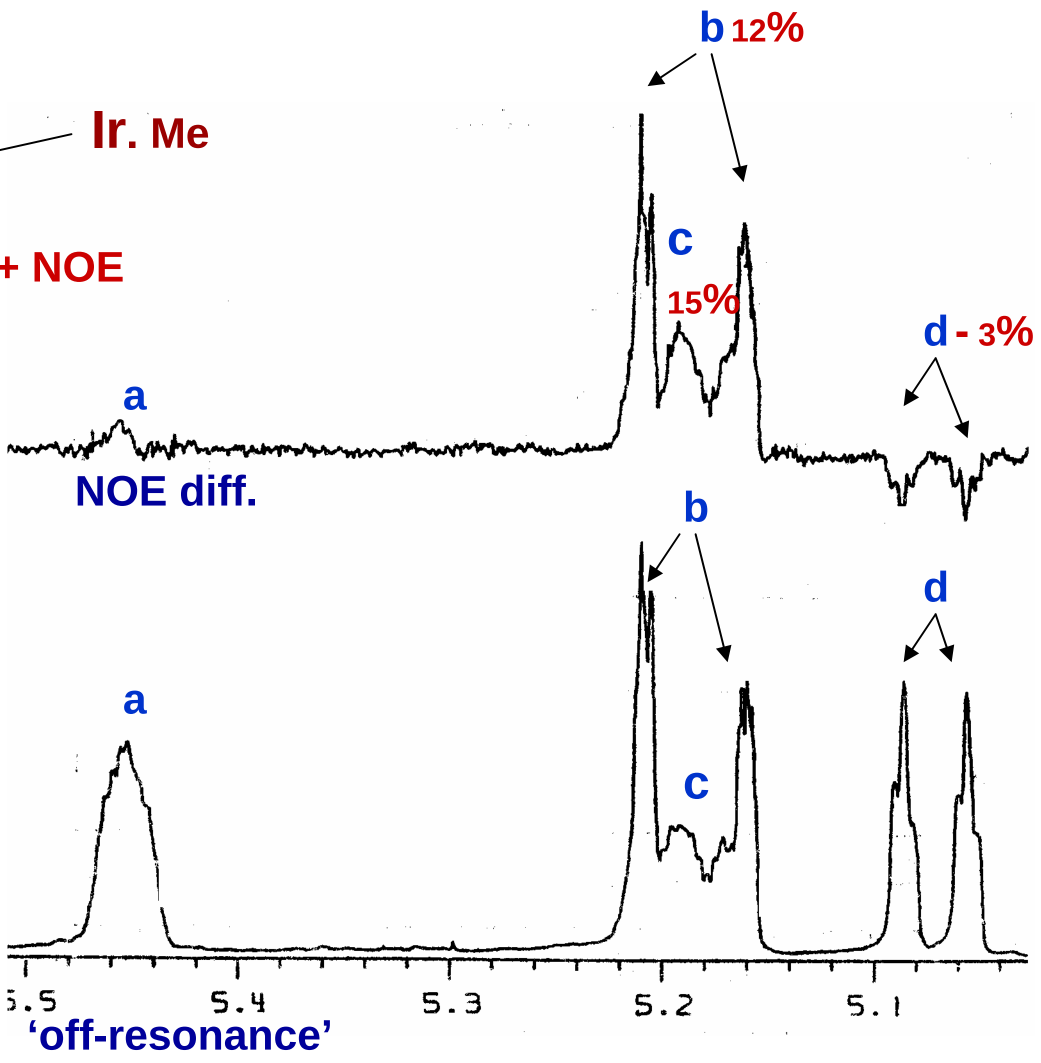


Distinguishing between citraconic acid & mesaconic acid using 1D NOE difference spectra

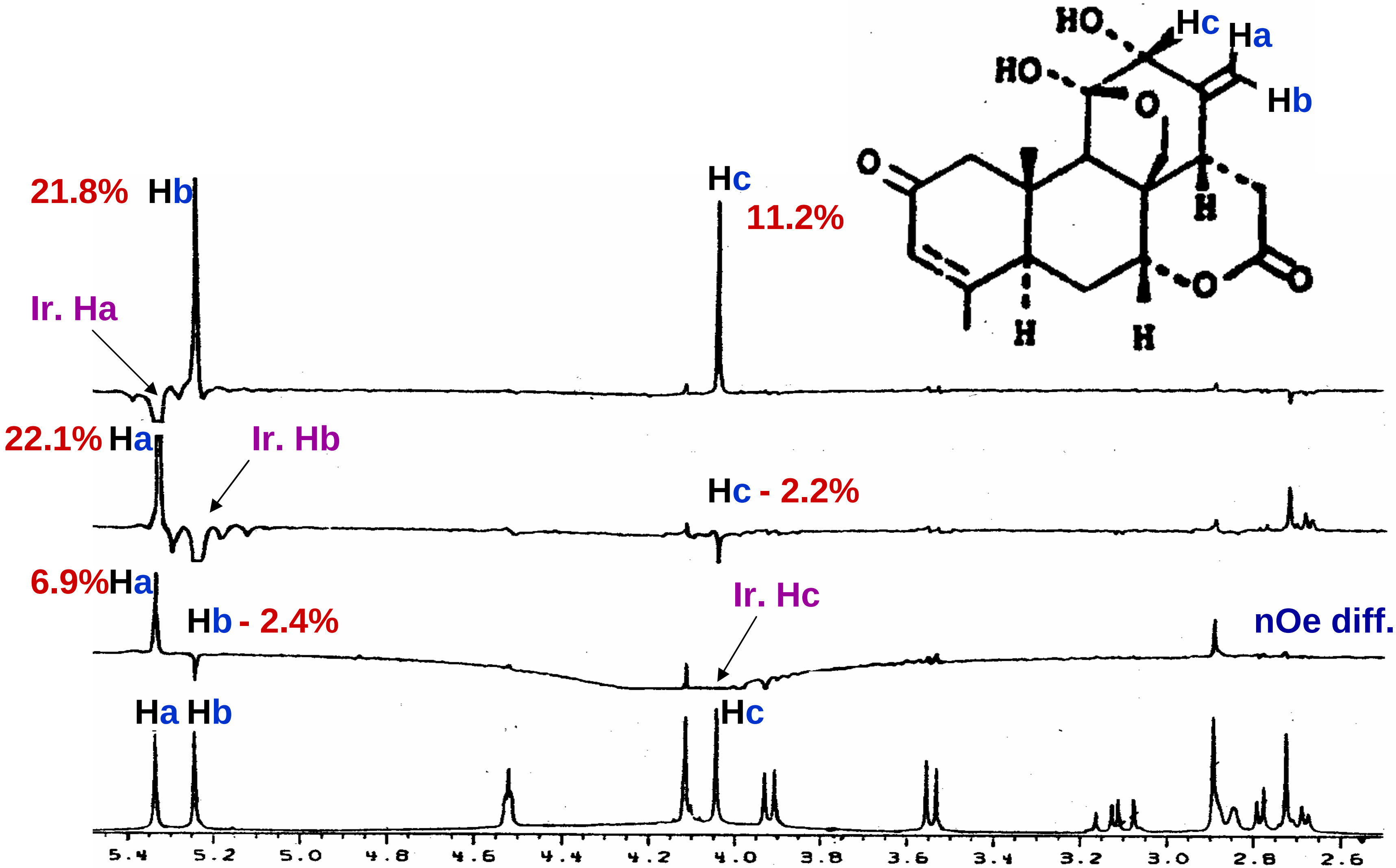


1D NOE Difference Spectra

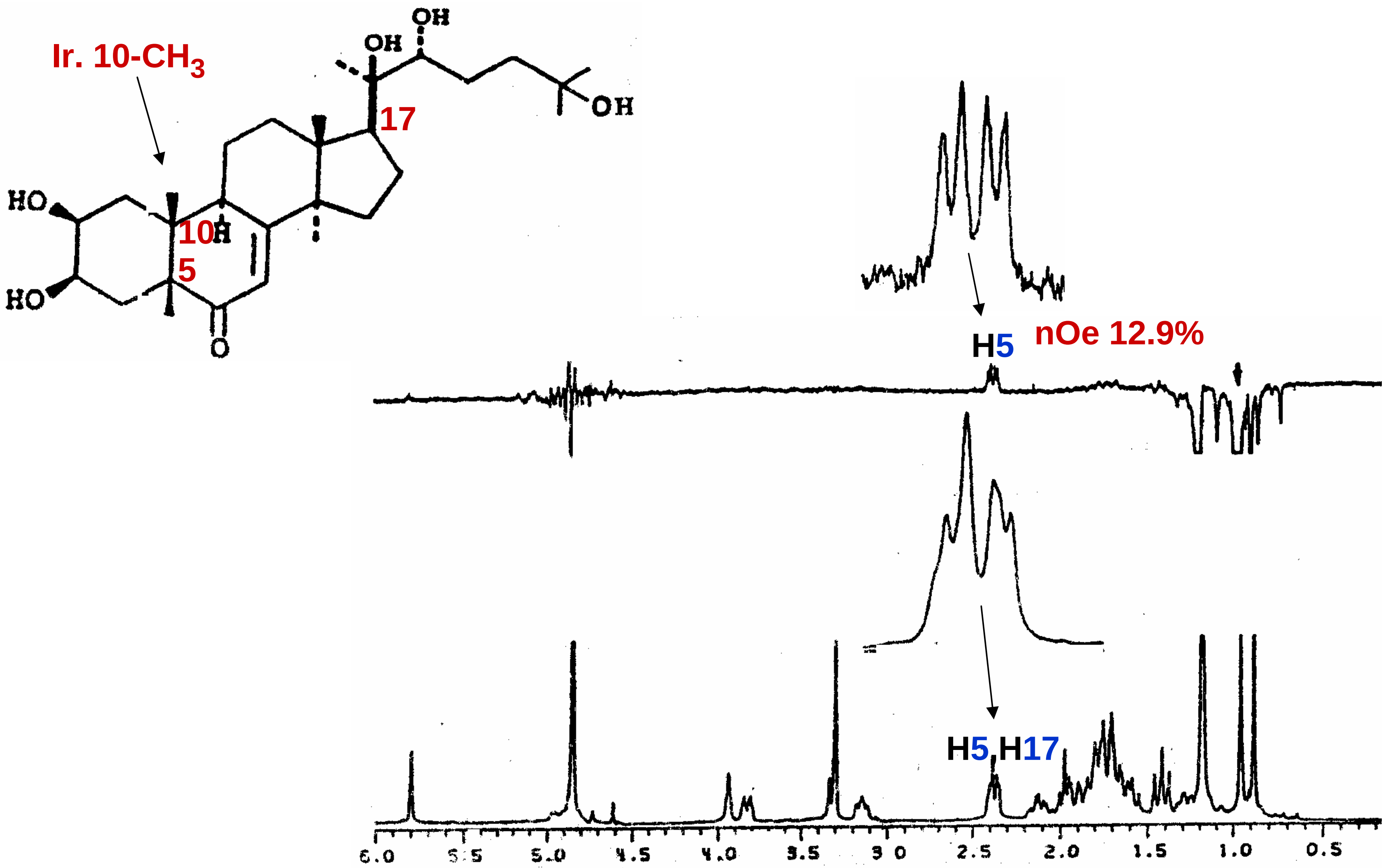




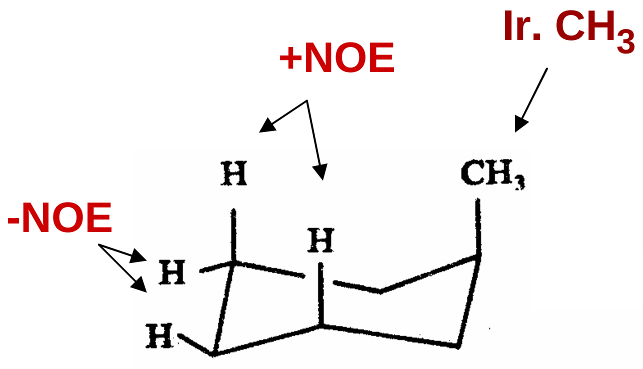
1D NOE Difference Spectra

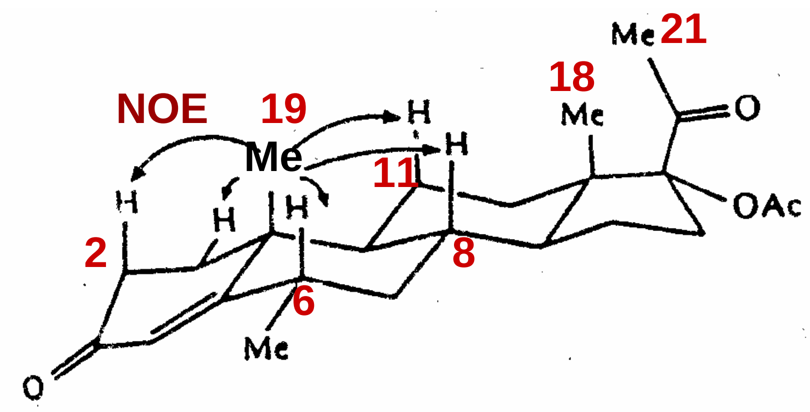


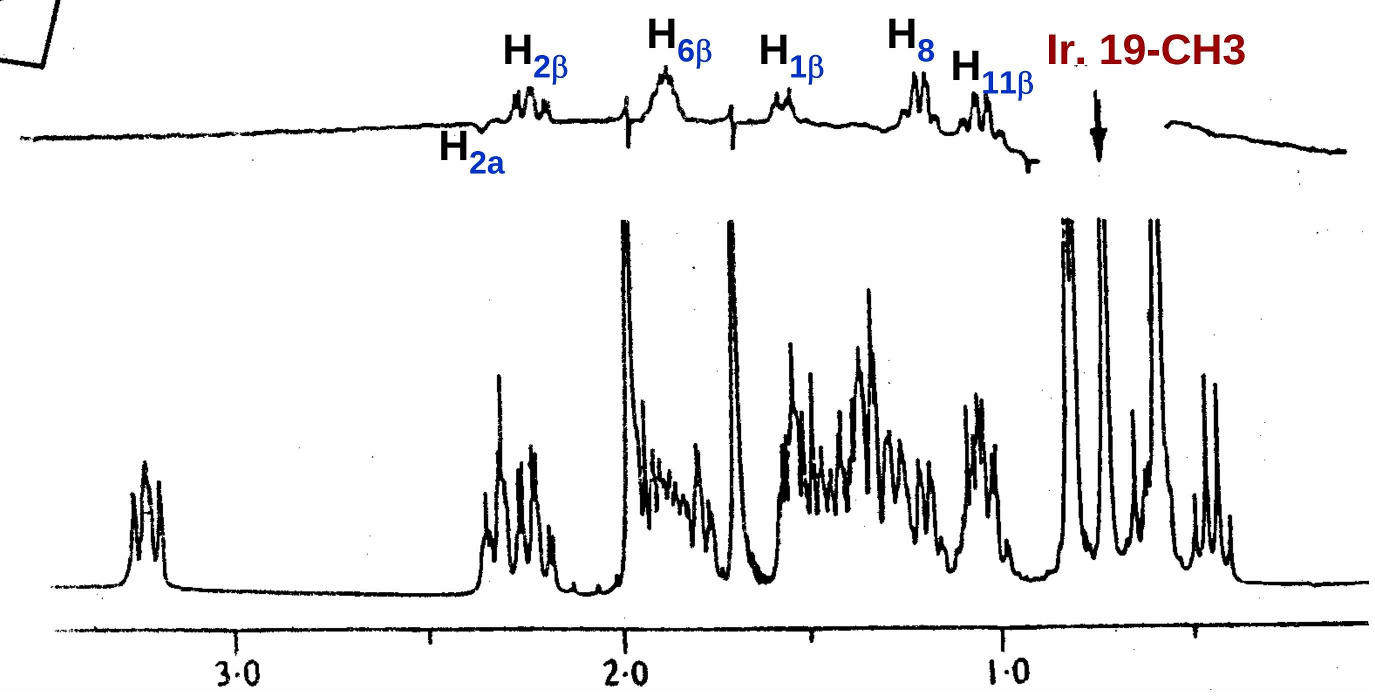
1D NOE Difference Spectra



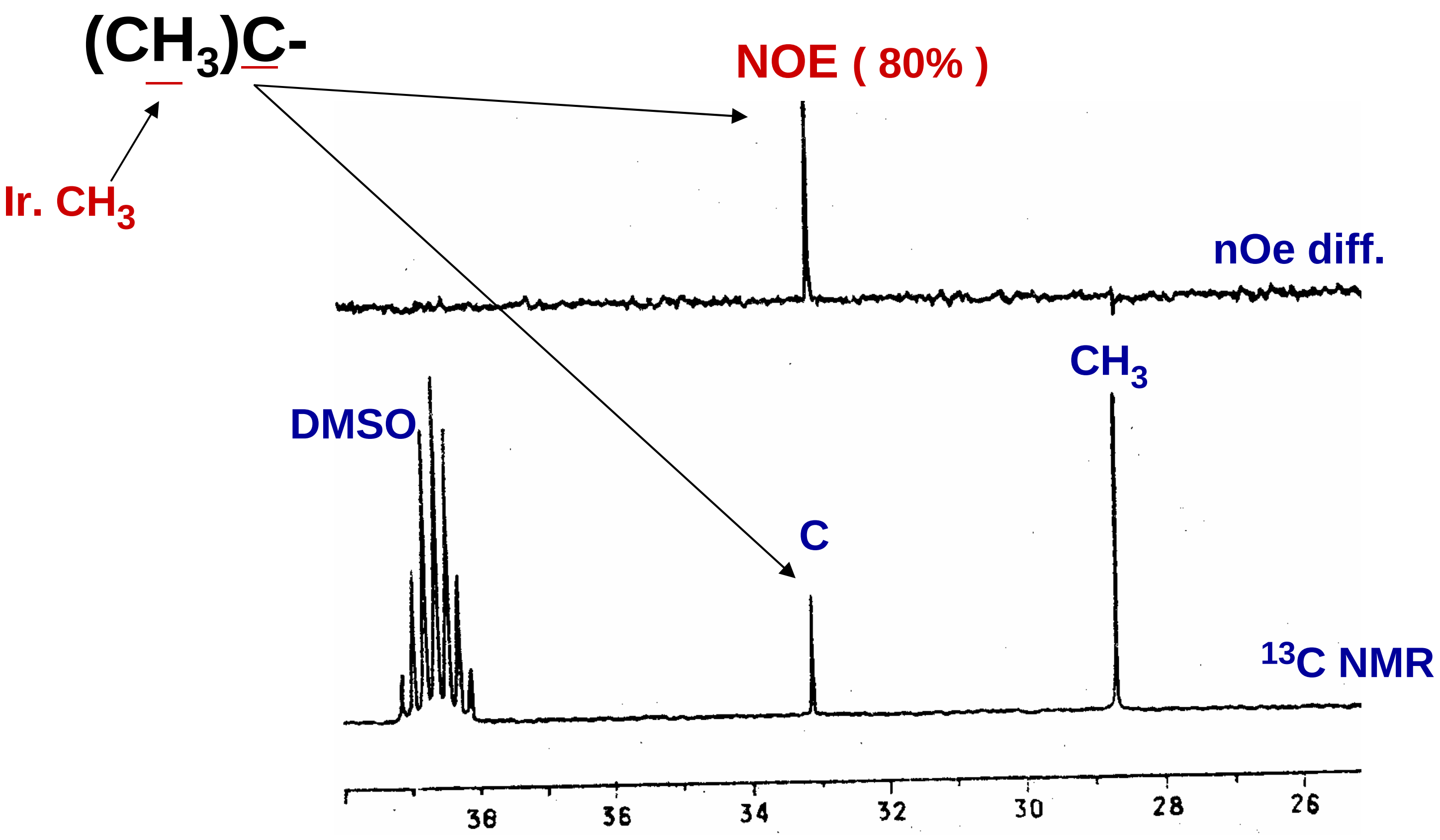
1D NOE Difference Spectra



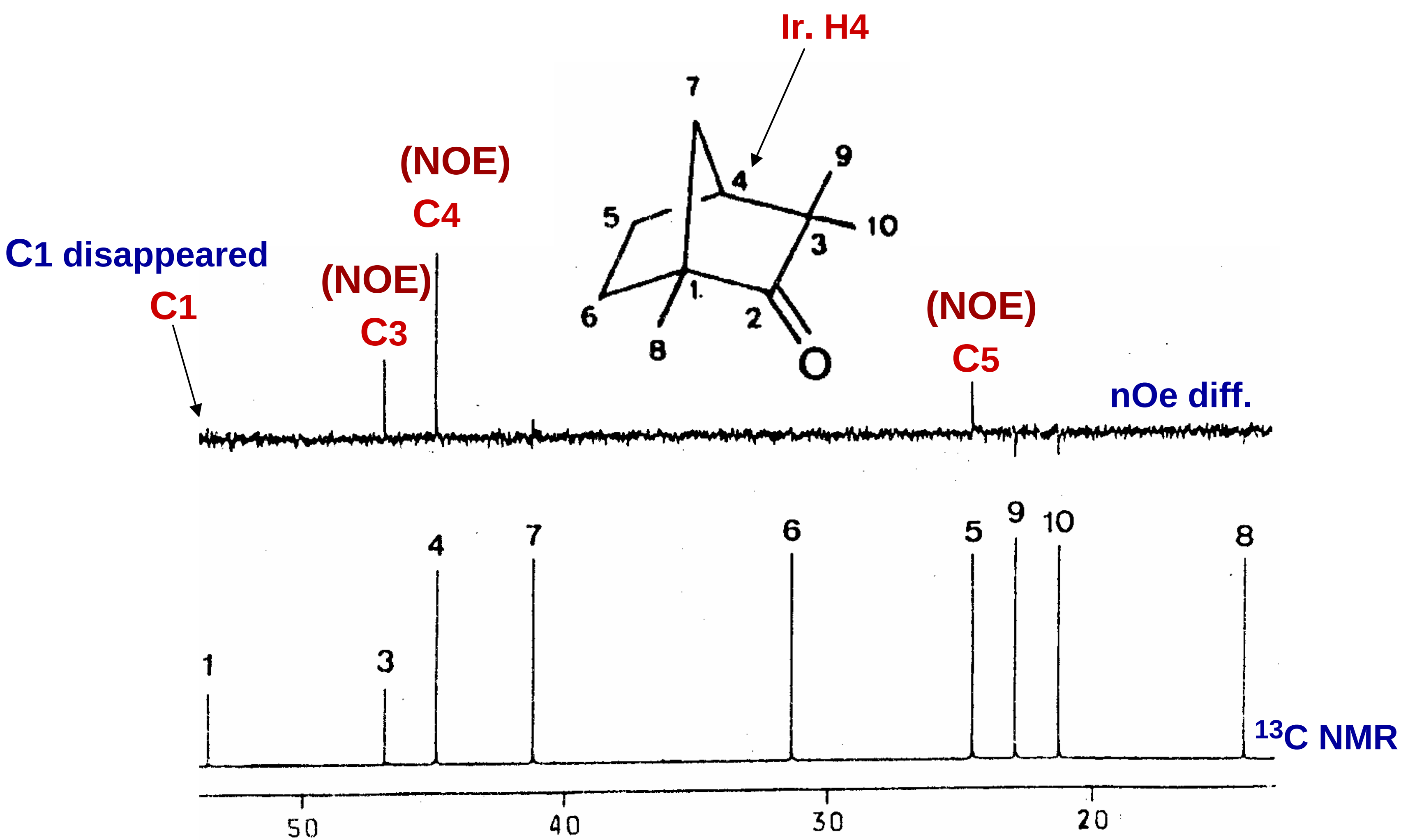




Selective heteronuclear ^{1}H-^{13}C NOE Difference Spectra on a compound containing a *t*-butyl group



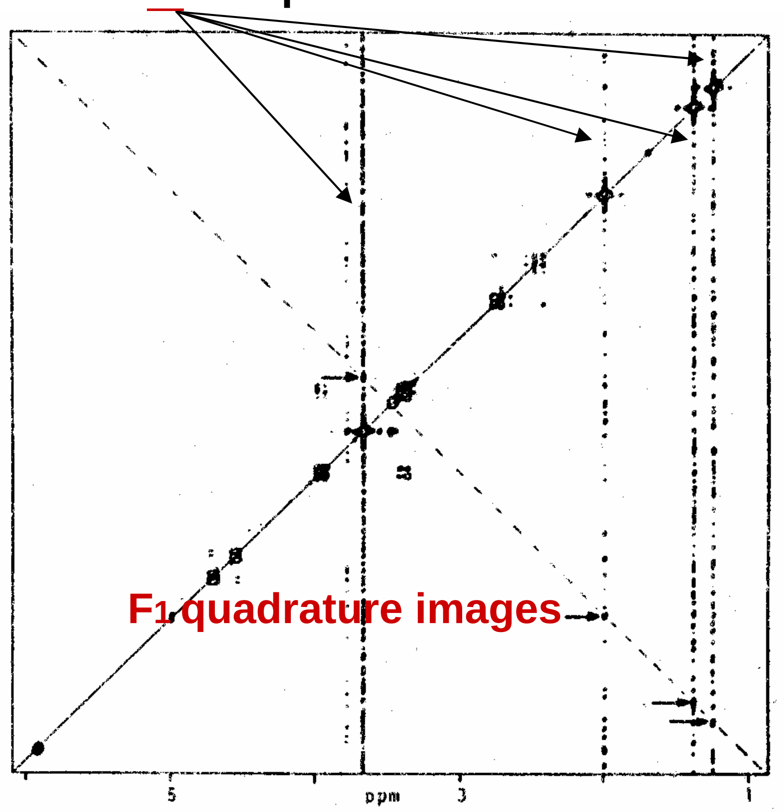
Selective heteronuclear ^{1}H-^{13}C NOE Difference Spectra



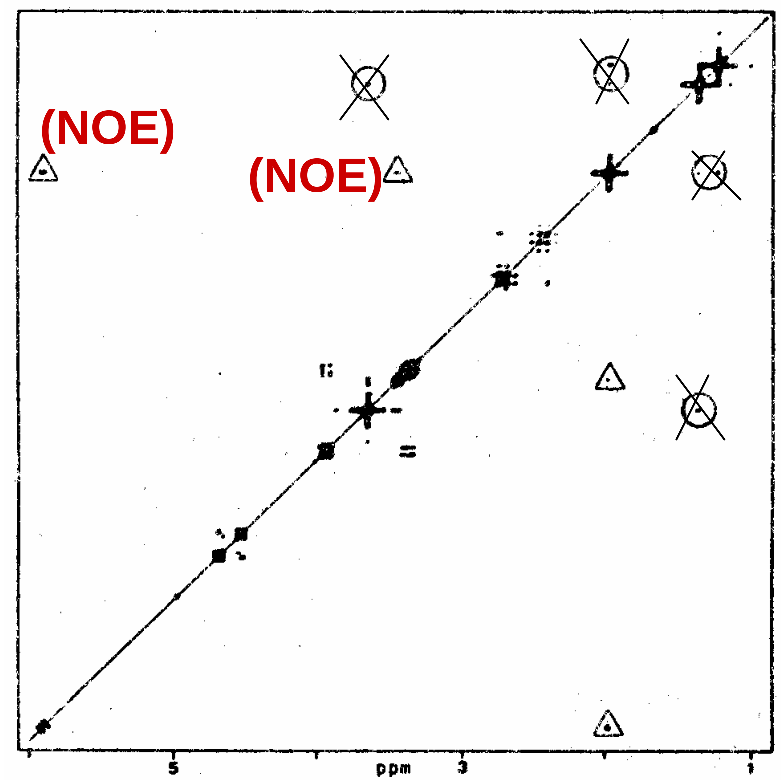
2D ^1H -^1H NOESY

(Nuclear Overhauser and Exchange SpectroscopY)

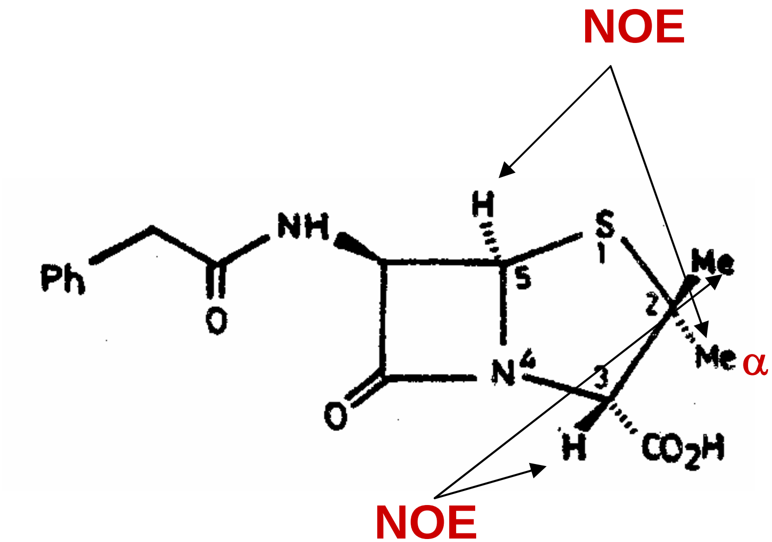
F1 noise strips for the four CH_3

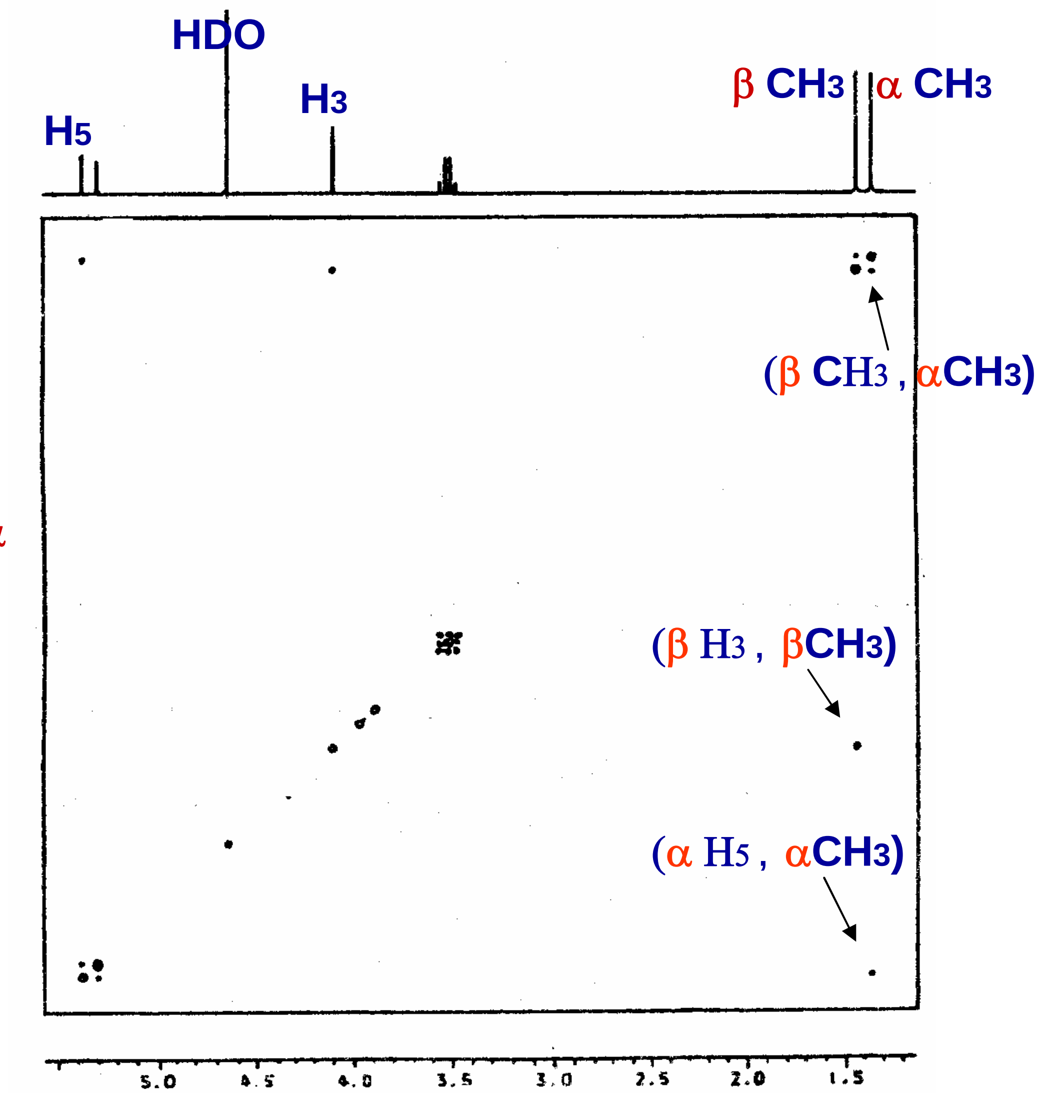


Symmetrization artifacts in NOESY

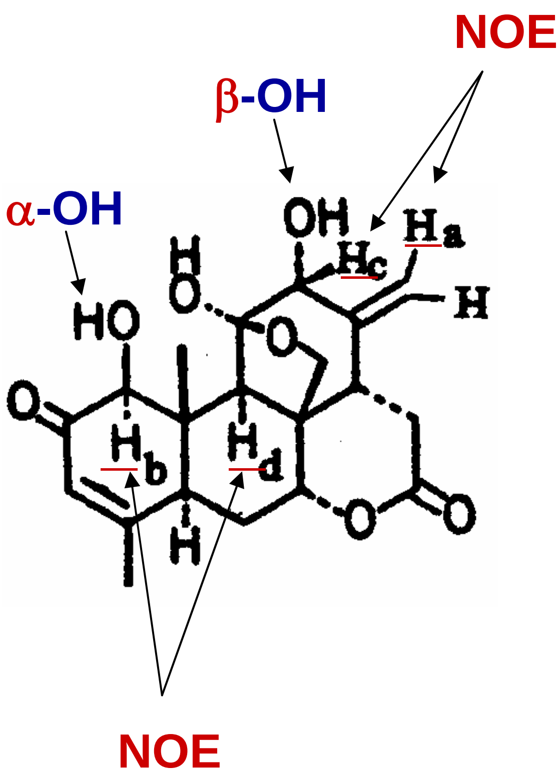


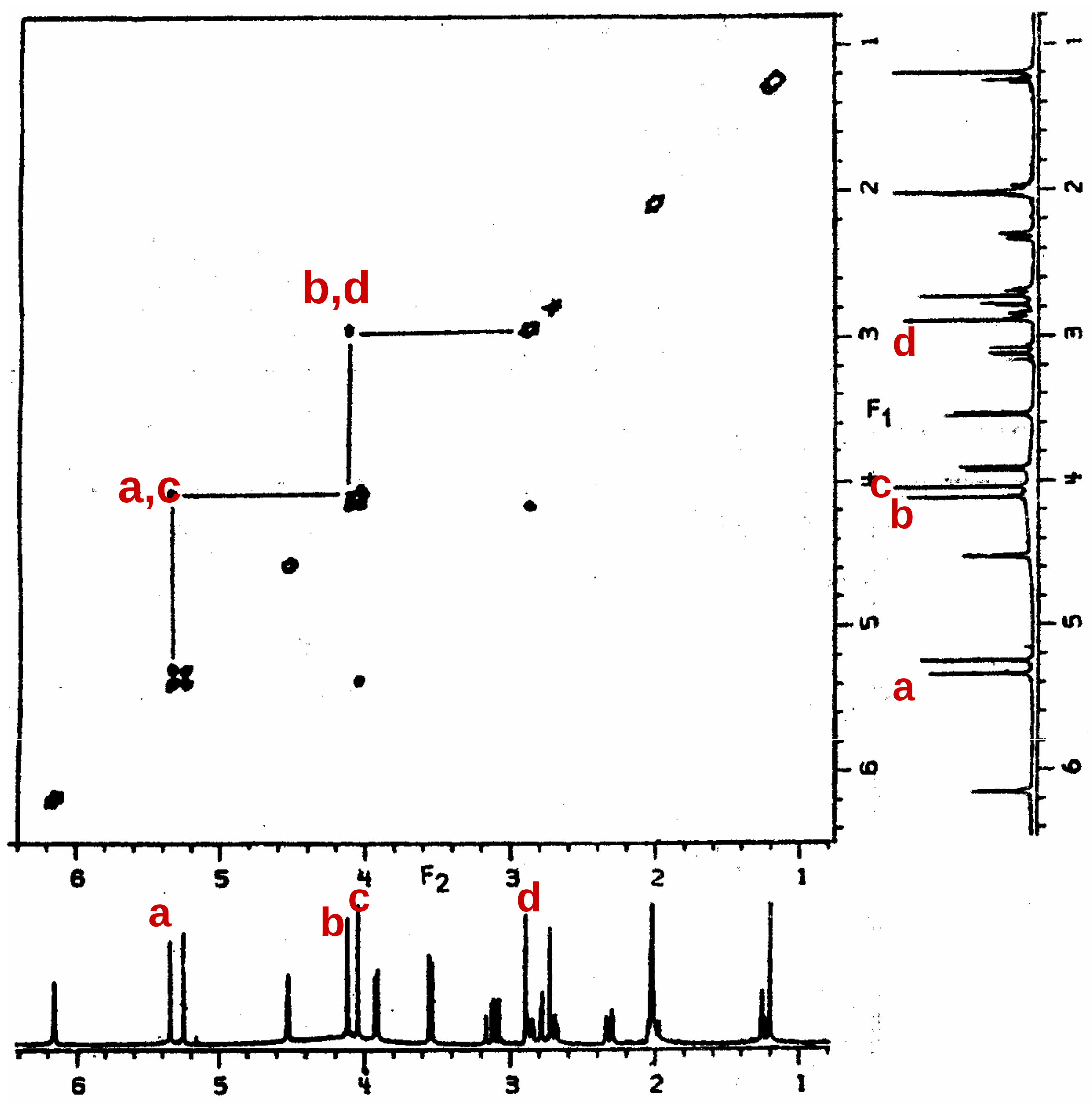
2D NOESY spectrum of a penicillin derivative



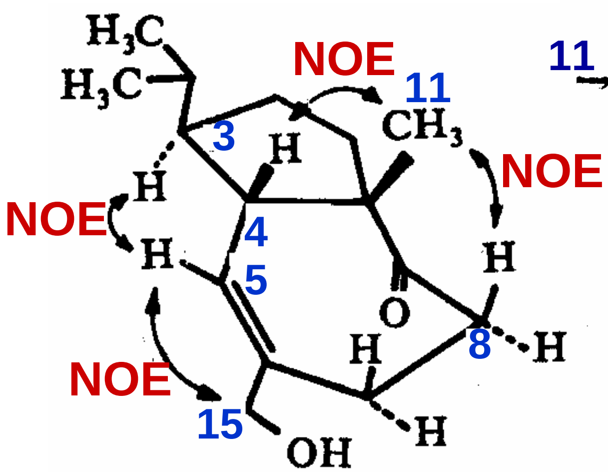


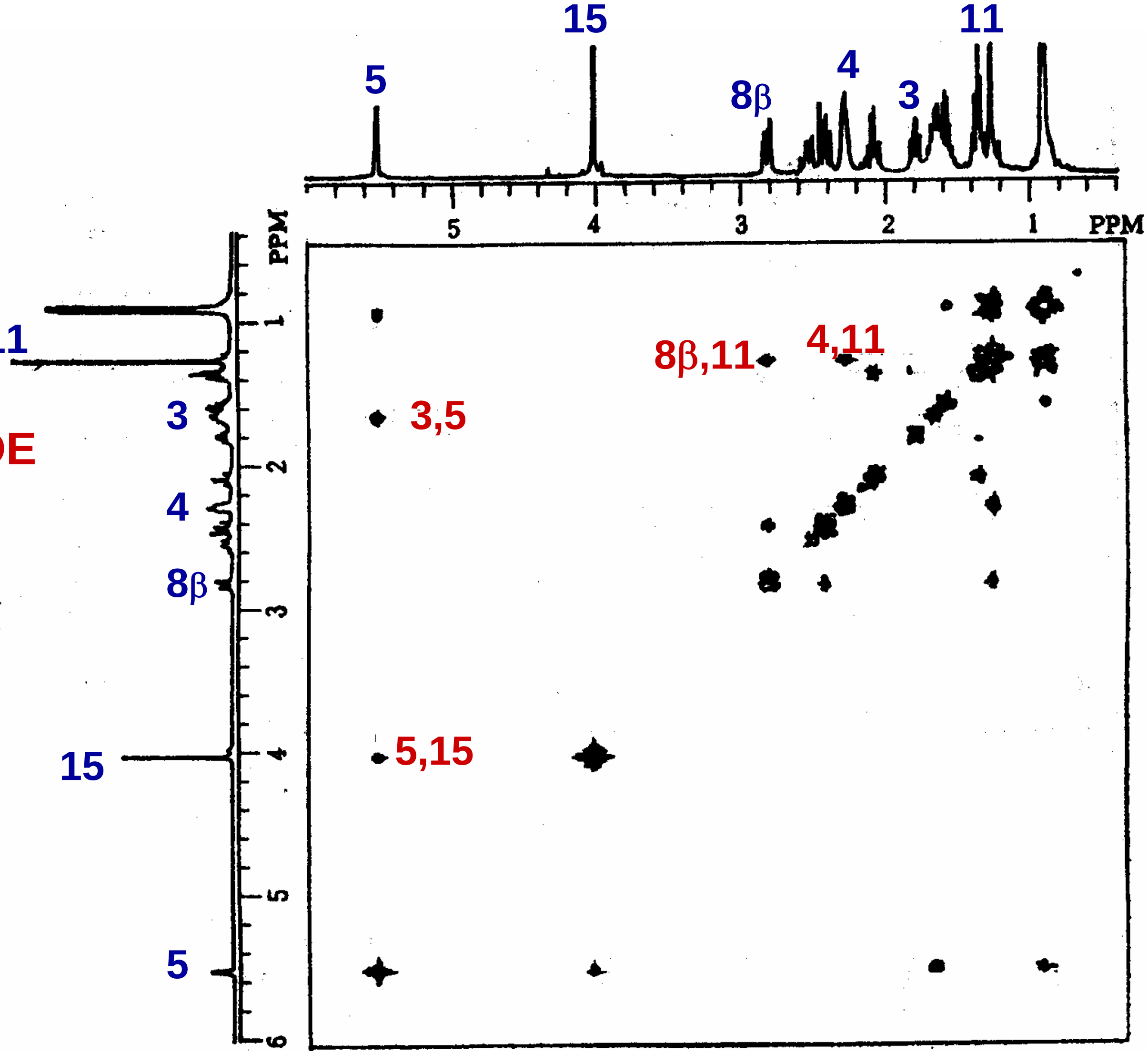
2D NOESY spectrum of ailanthone





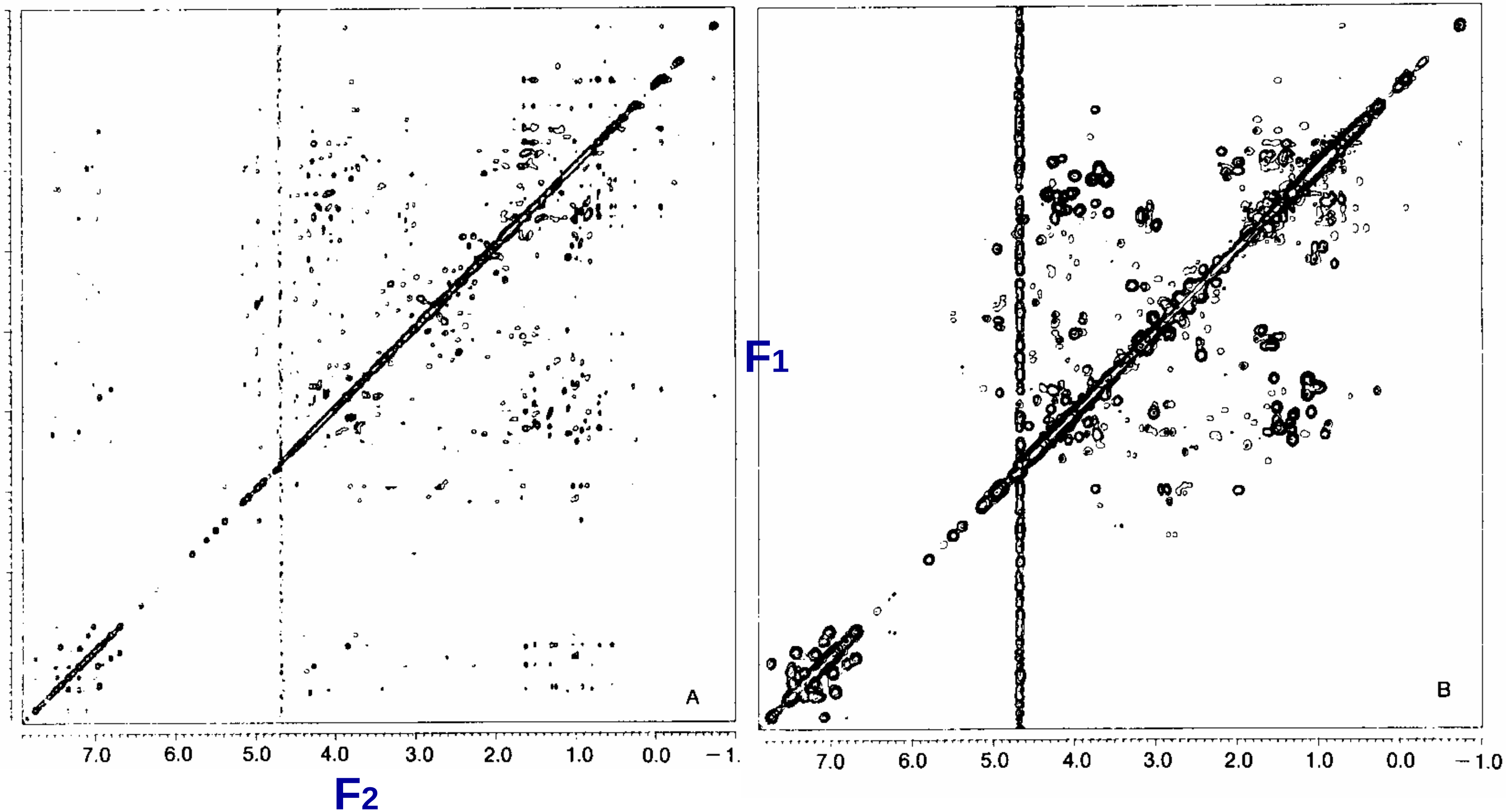
2D NOESY spectrum of aphanamol





Comparison of phase-sensitive NOESY and COSY- 90º spectra of lysozyme

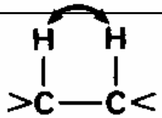
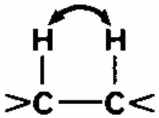
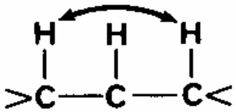
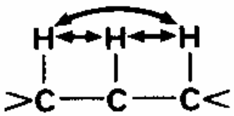
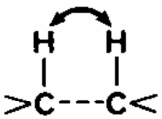
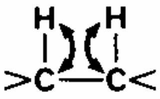
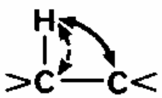
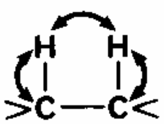
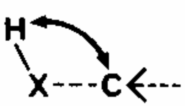
phase-sensitive NOESY | **COSY- 90º**



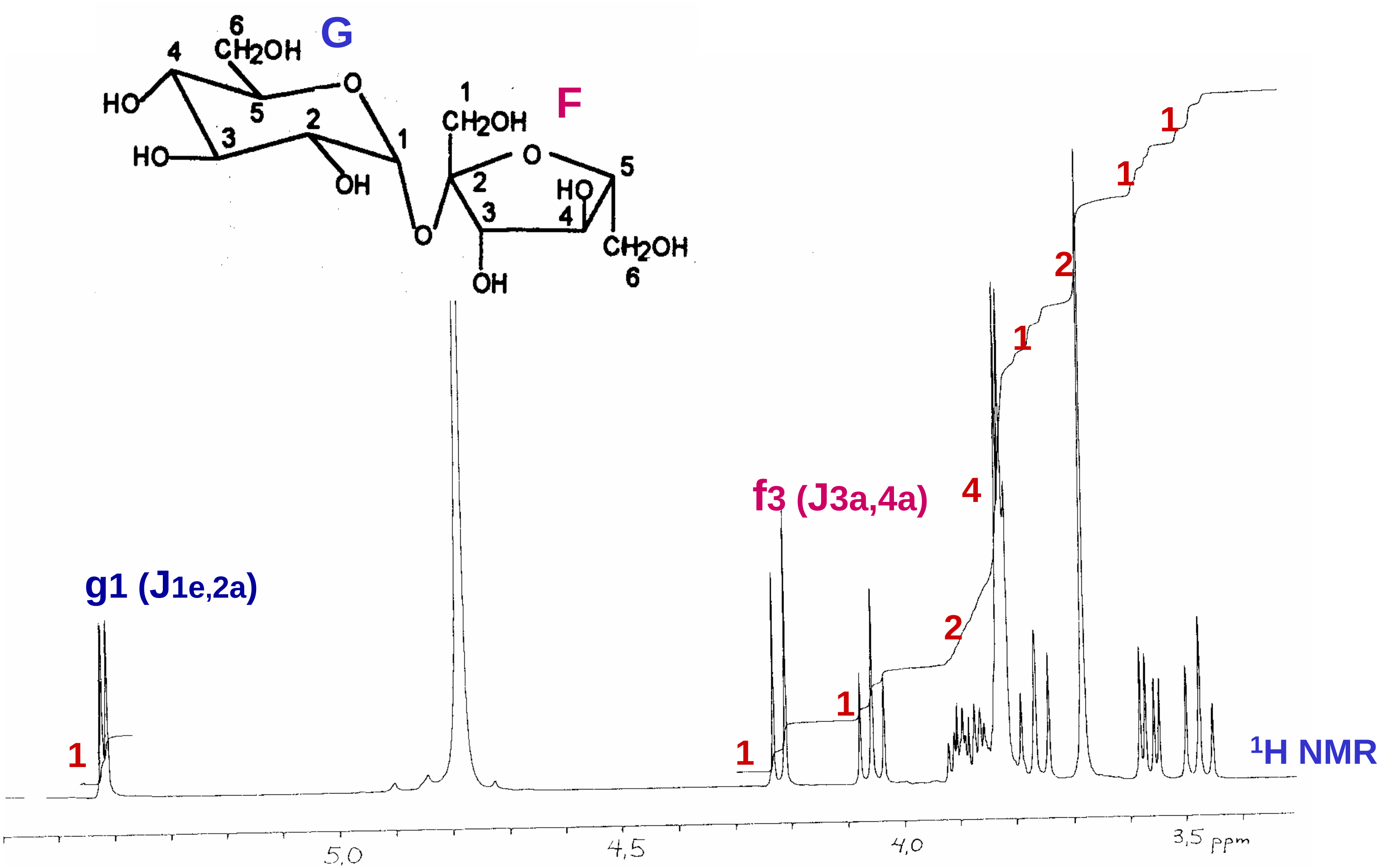
Chapter 11

Assigning molecular structures using one and two-dimensional NMR data

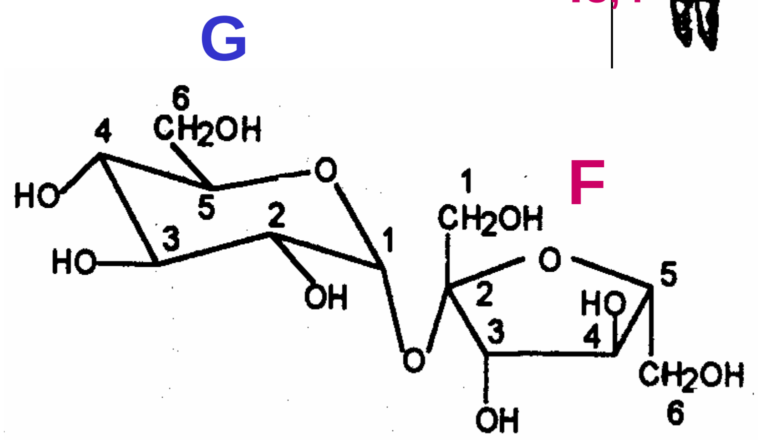
Some selected 2D NMR experiments

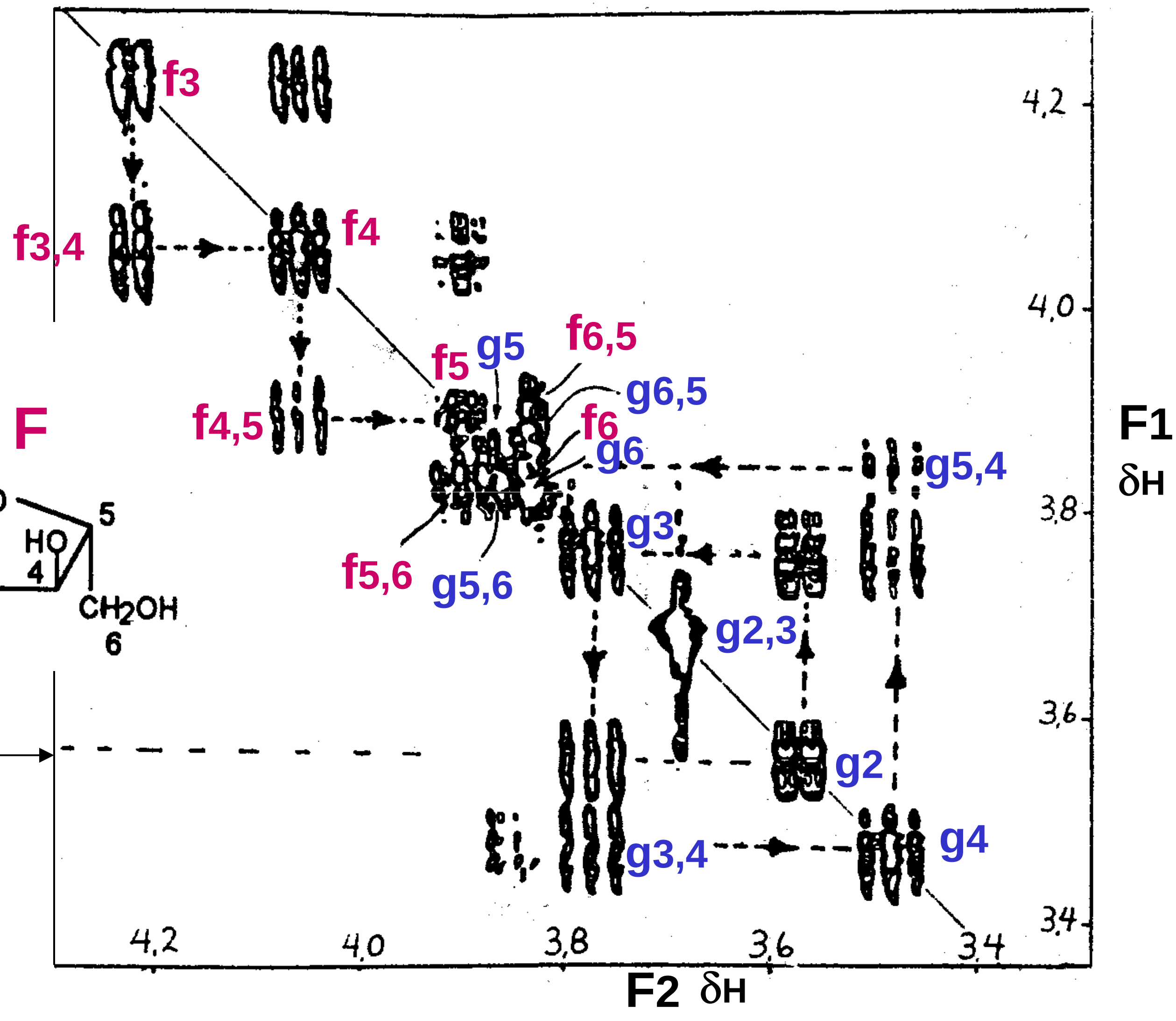
experiments	F1	F2		mechanism
1. Homonuclear H,H 2d J-δ	δ_H	J_{HH}		$^{n}J_{HH}$ (n>2)
2. H,H COSY	δ_H, J_{HH}	δ_H,J_{HH}		$^{n}J_{HH}$ (n=2,3)
3. Long range COSY	δ_H,J_{HH}	δ_H,J_{HH}		$^{n}J_{HH}$ (n>3)
4. H,H relay	δ_H,J_{HH}	δ_H,J_{HH}		$^{n}J_{HH}$ (n=2,3)
5. NOESY (1D nOe diff.)	δ_H, J_{HH}	δ_H, J_{HH}		nOe ($=f.r_{HH}^{-6}$)
6. C,H COSY (HMQC)	δ_C	δ_H,J_{HH}		$^{1}J_{CH}$
7.Long-range C,H COSY (COLOC) (HMBC)	δ_H	δ_H		$^{n}J_{CH}$ (n>1)
8. Heteronuclear relay	δ_C	δ_H,J_{HH}		$^{n}J_{CH}$ (n=2,3); $^{1}J_{CH}$
9. HOESY	δ_C	δ_H,J_{HH}		nOe ($=f.r_{CH}^{-6}$)
10. 2D- INADEQUATE	δ_C, J_{CC}	F1 D.Q F2 δ_C		$^{1}J_{CC}$

Assigning ^{1}H NMR Spectrum of Sucrose

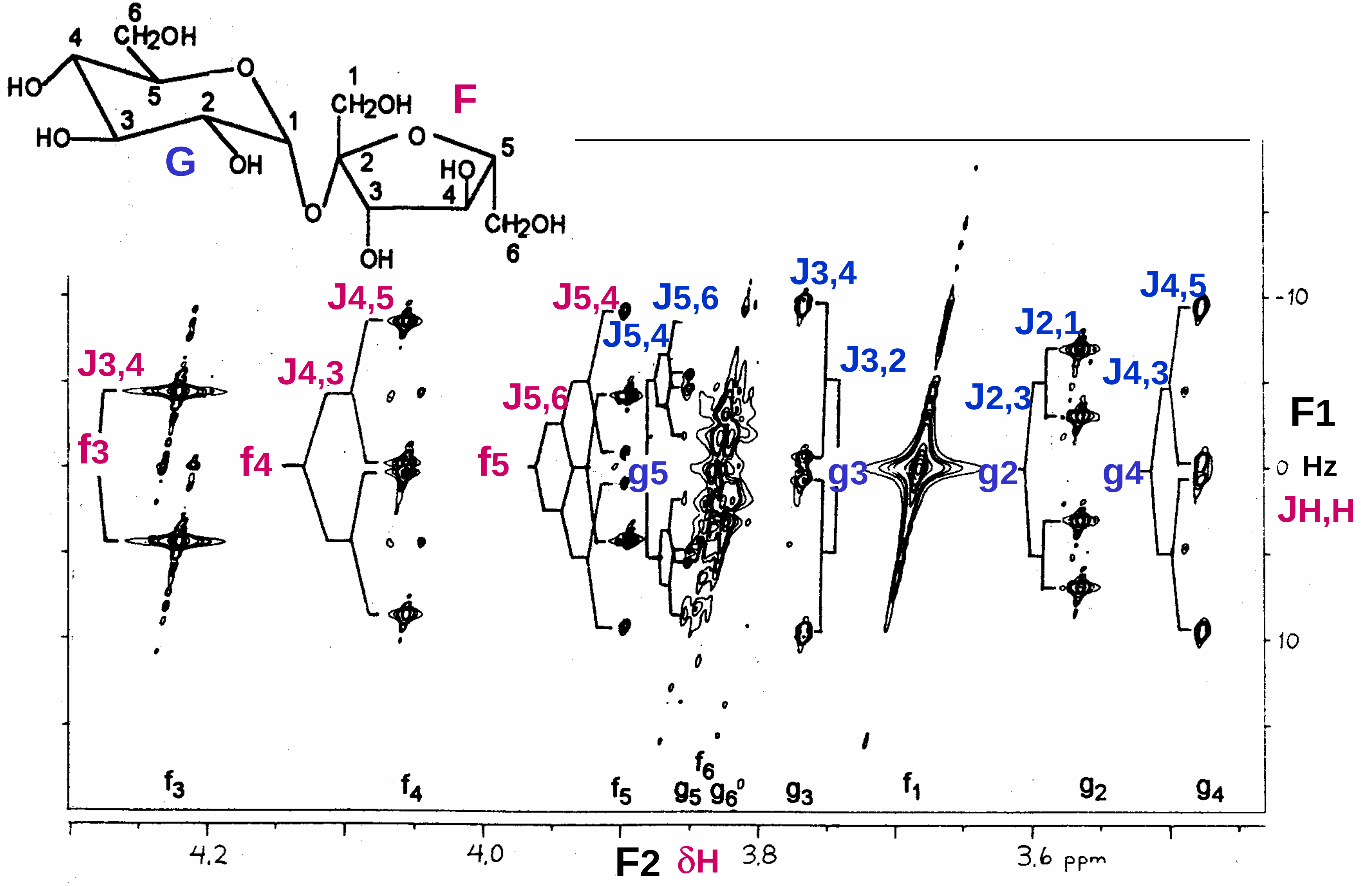


Assigning $^1H,^1H$ COSY 90° Spectrum of Sucrose

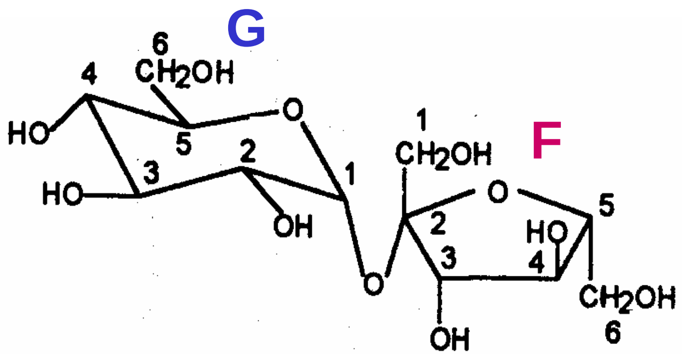


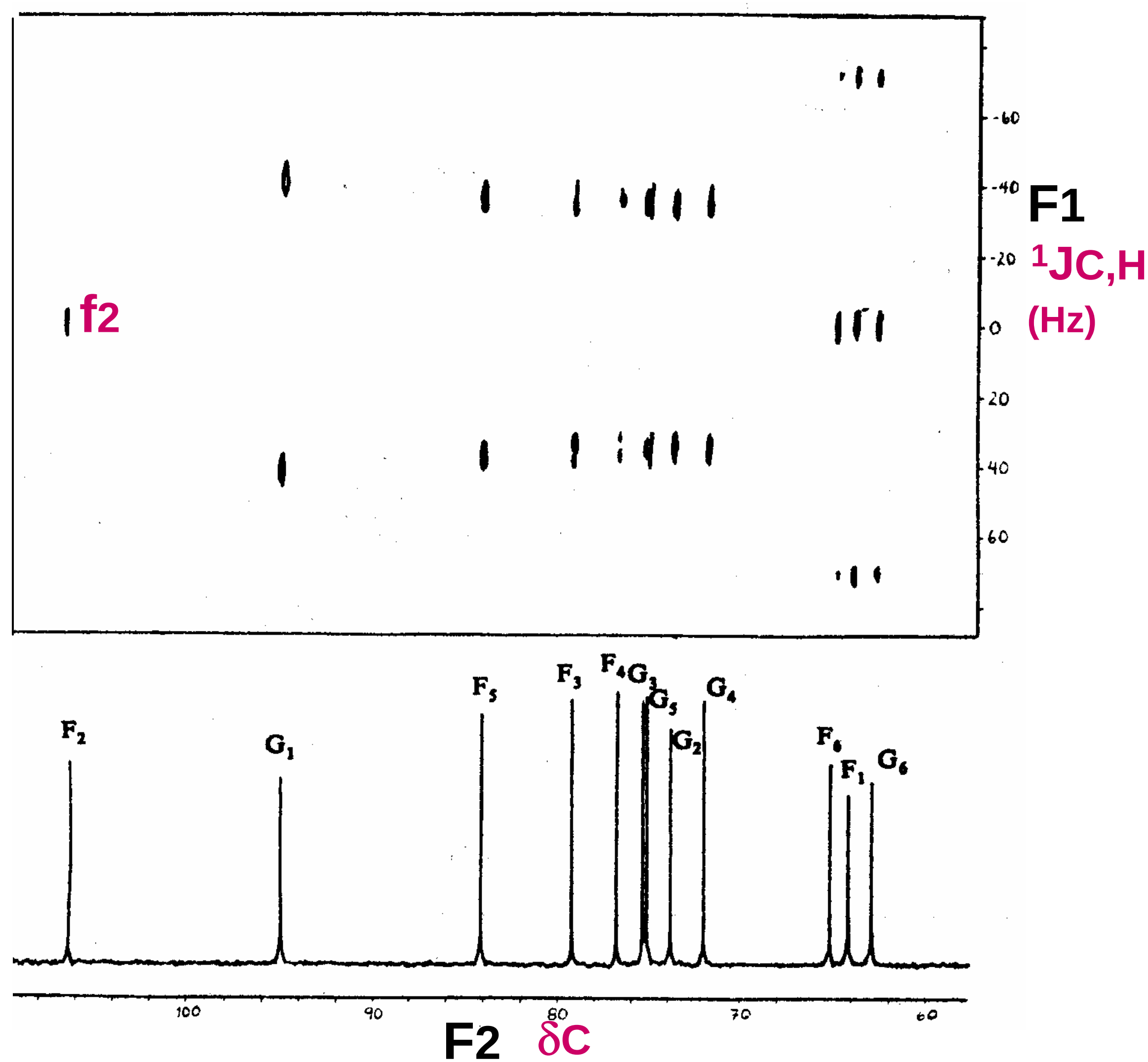


Assigning $^{1}H,^{1}H$ 2D J-δ Spectrum of Sucrose

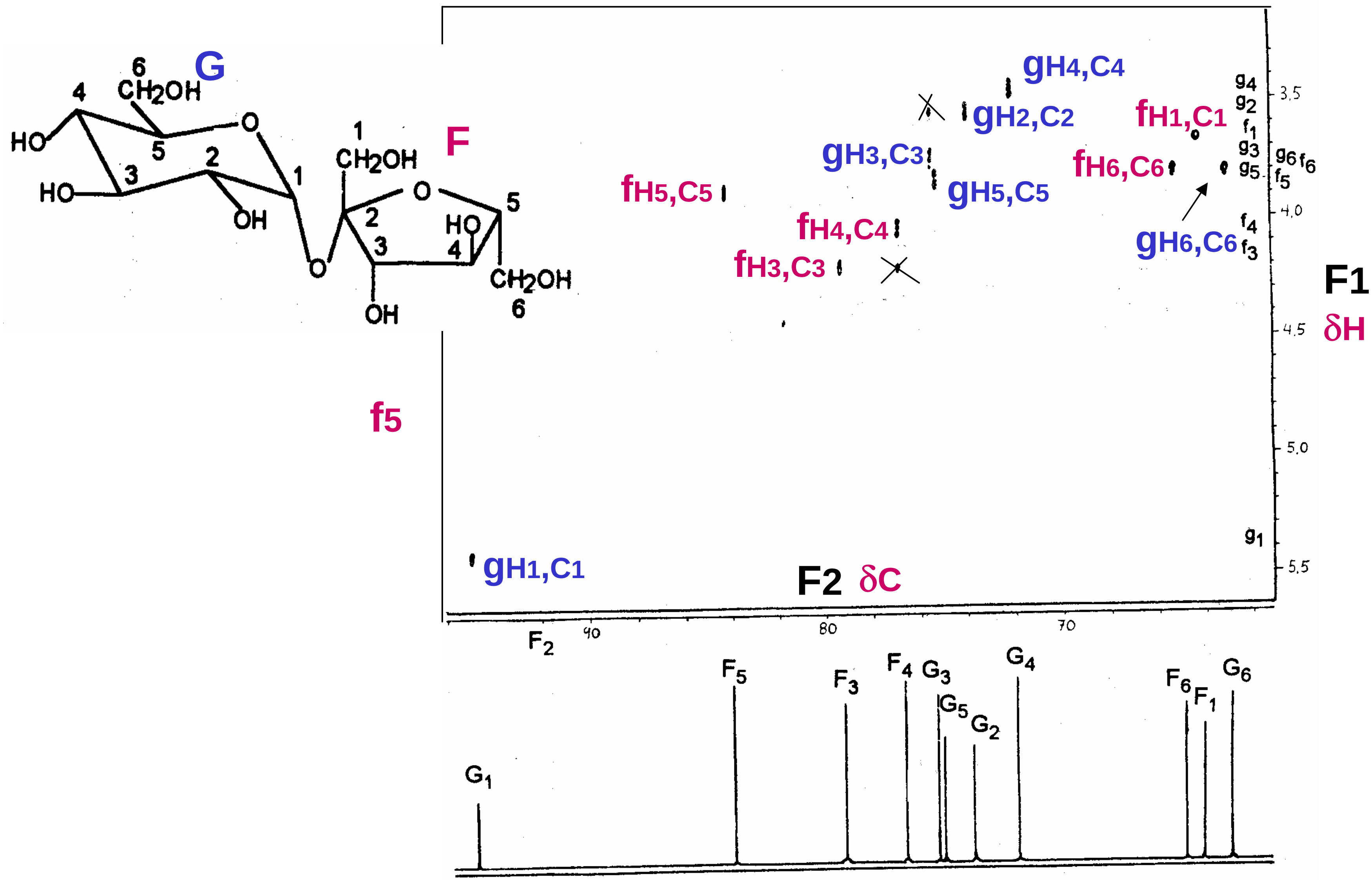


Assigning $^{13}C,^{1}H$ 2D J- δ Spectrum of Sucrose

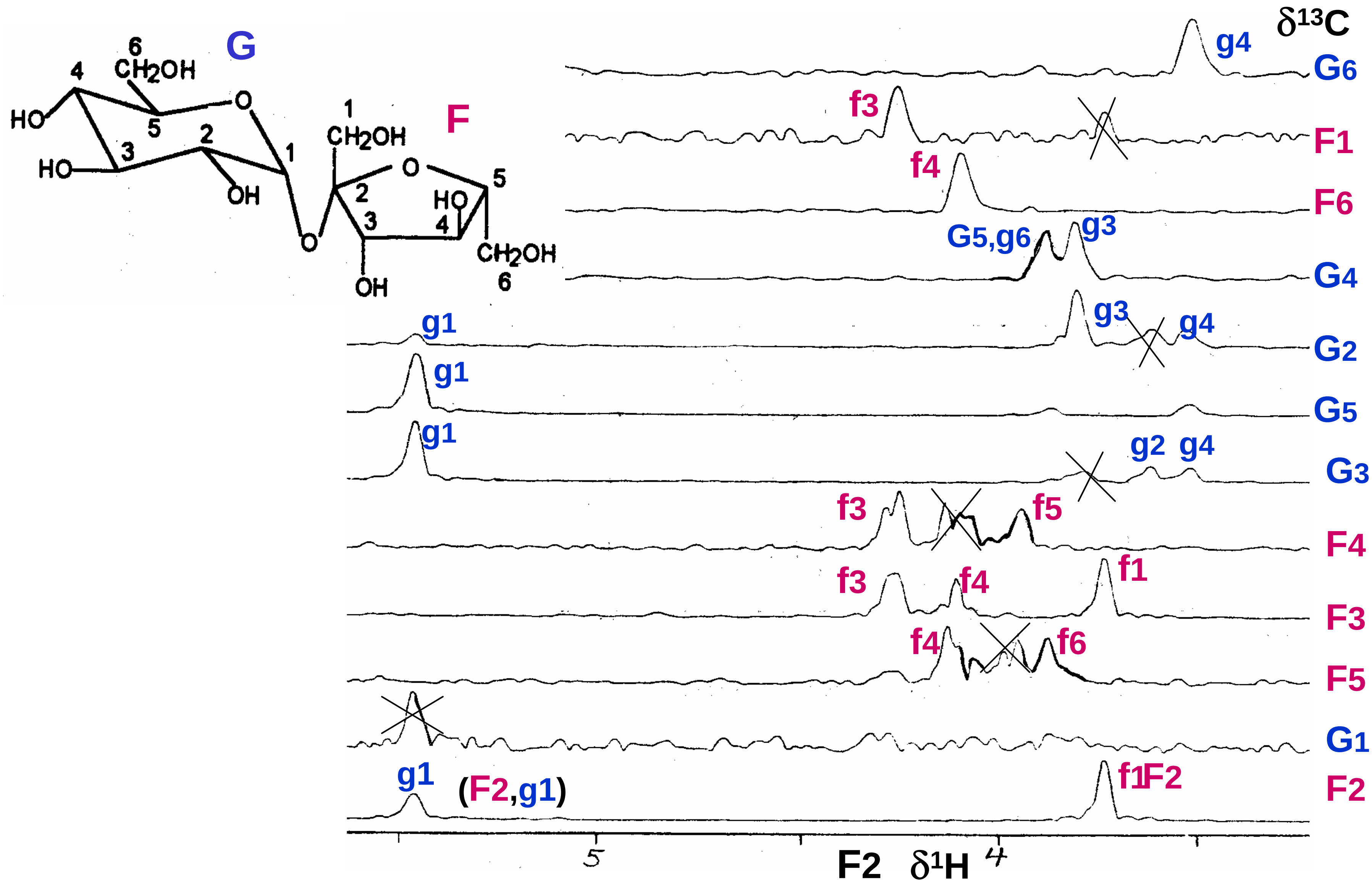




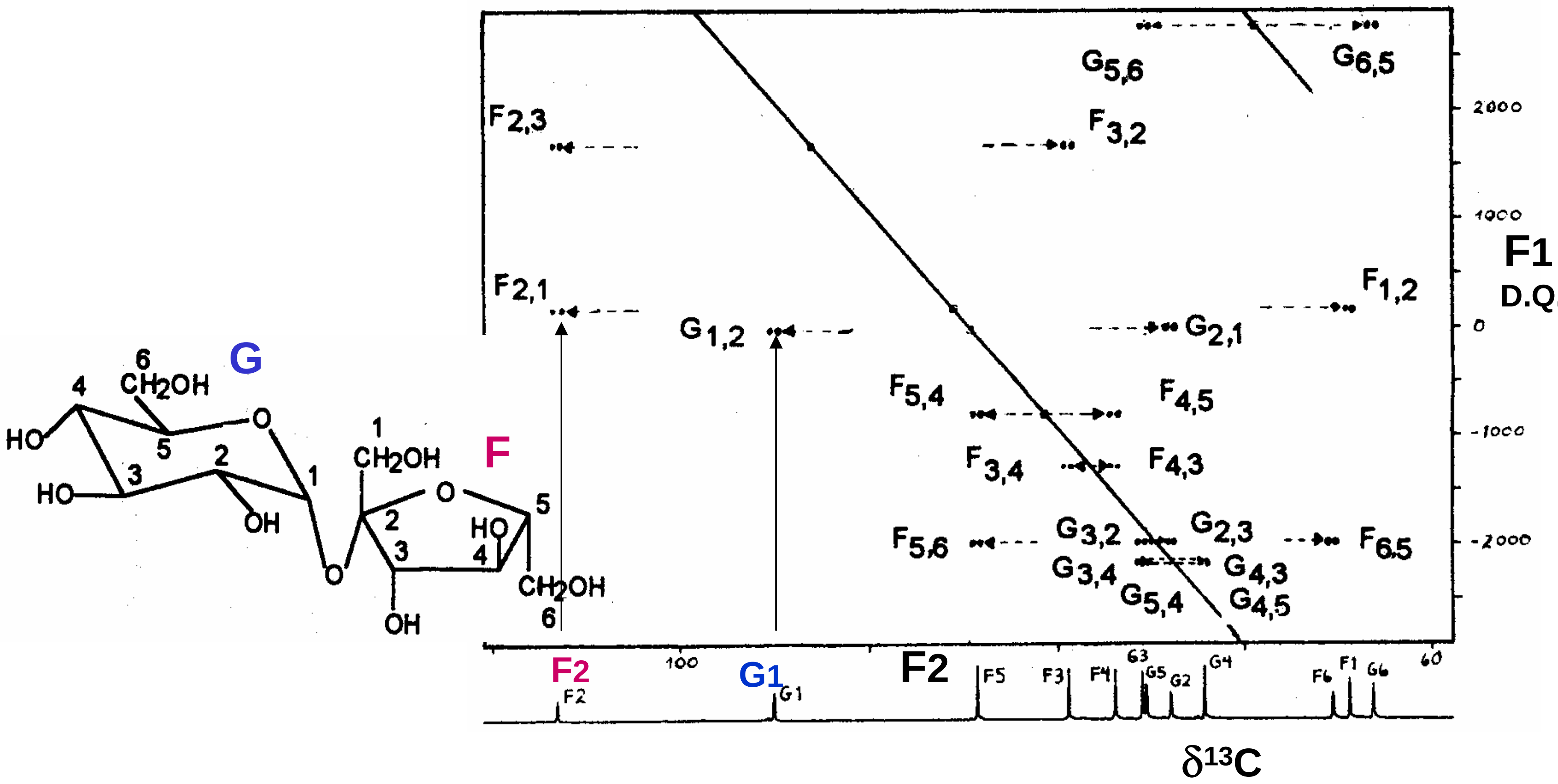
Assigning $^{13}C,^{1}H$ COSY Spectrum of Sucrose



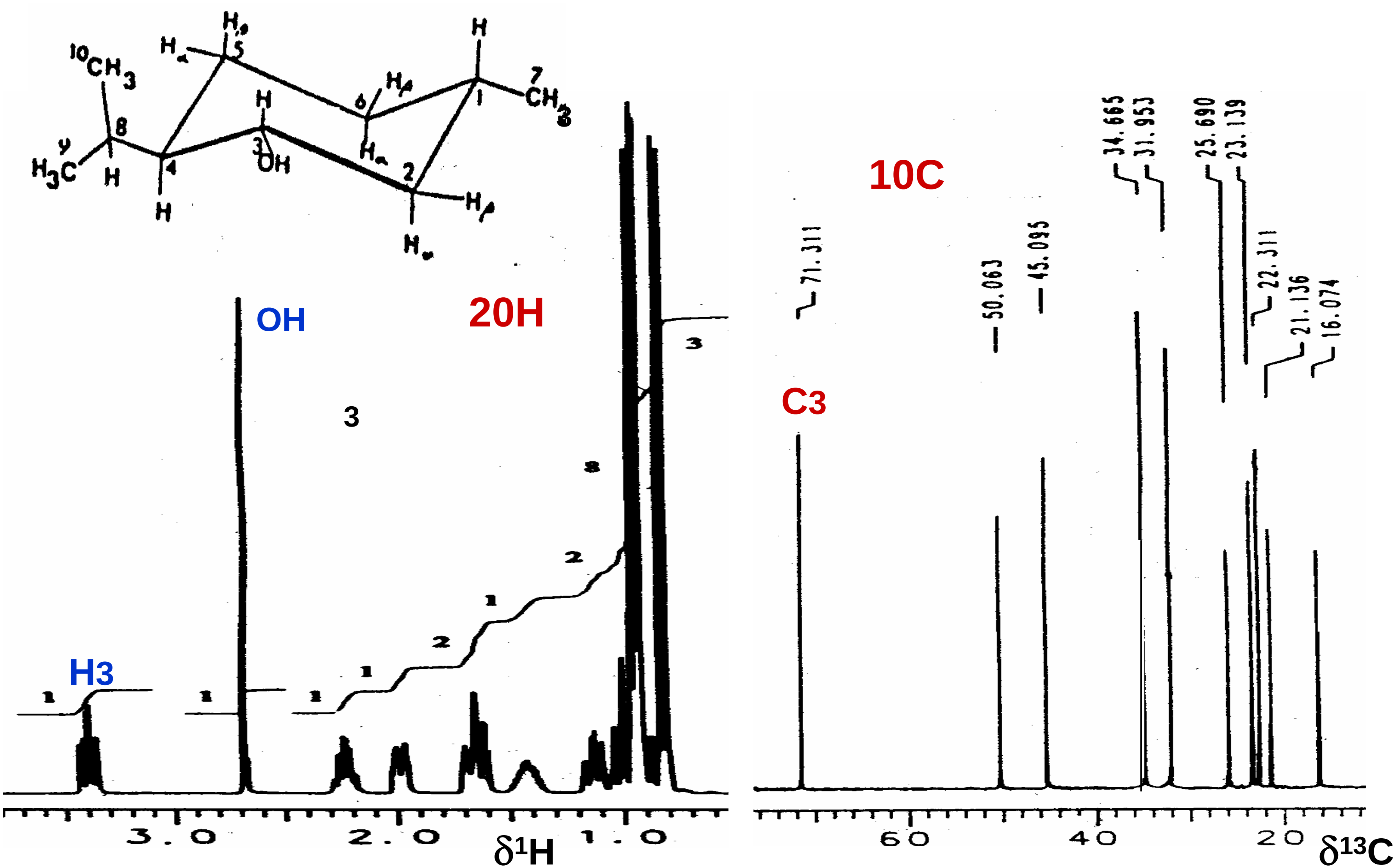
Assigning COLOC Spectrum of Sucrose



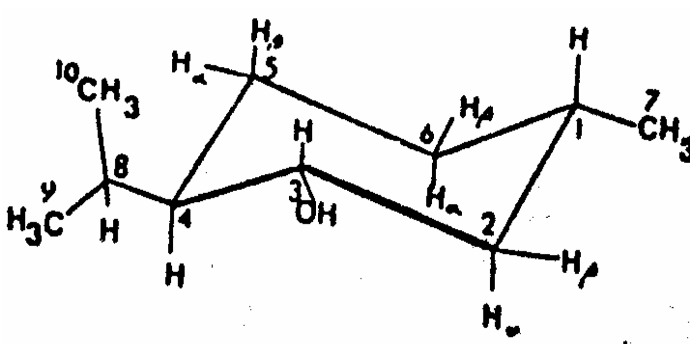
Assigning INADEQUATE Spectrum of Sucrose

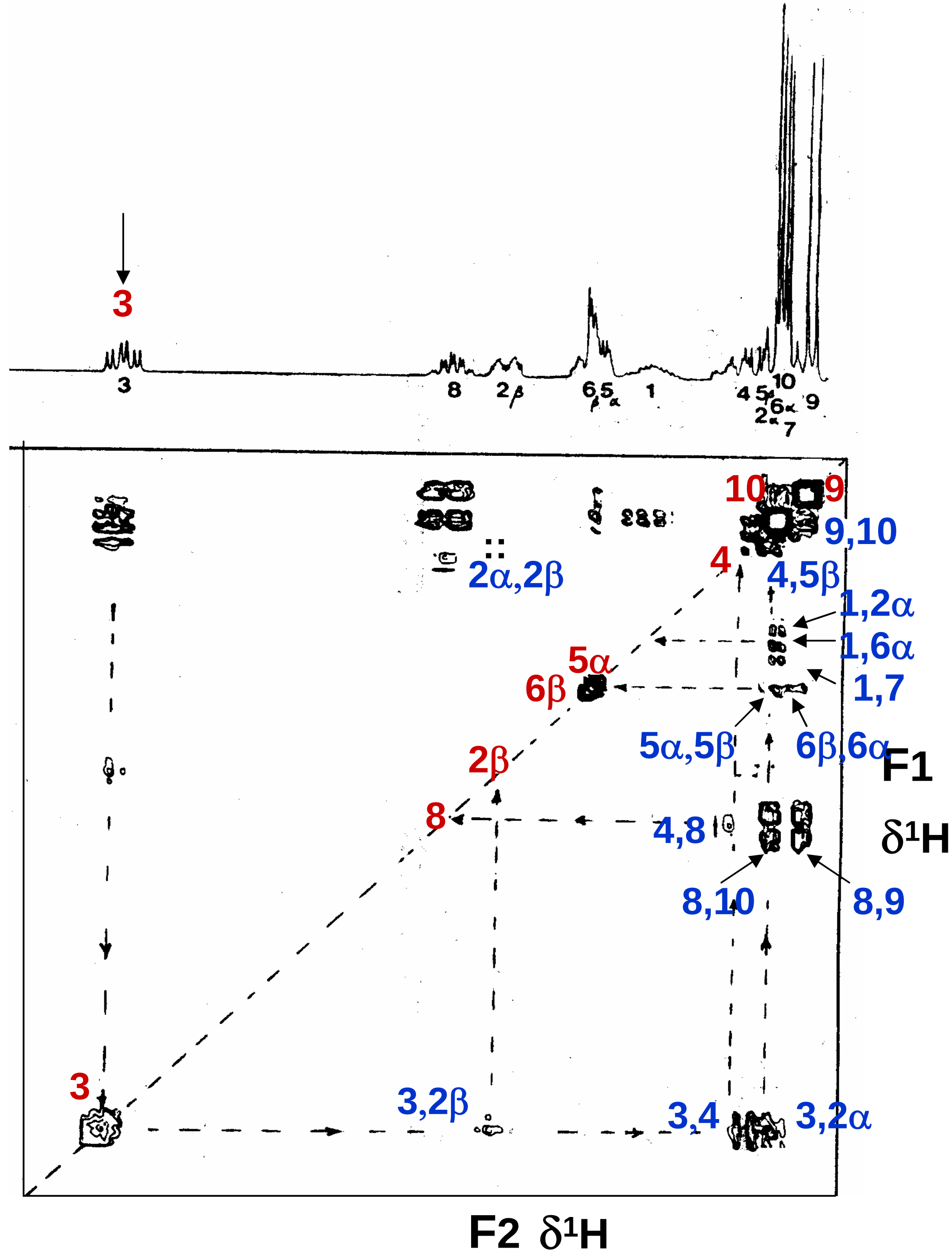


Assigning ^{1}H and ^{13}C NMR Spectra of Menthol

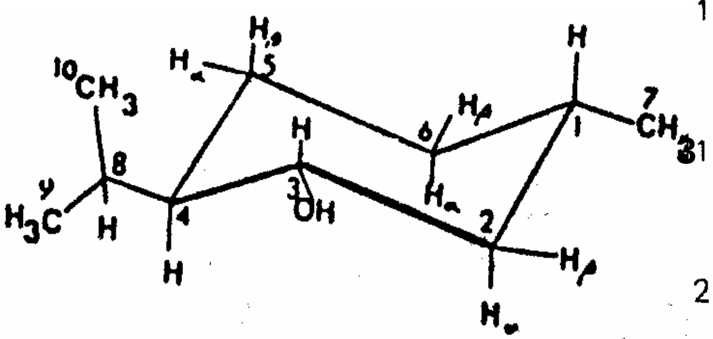


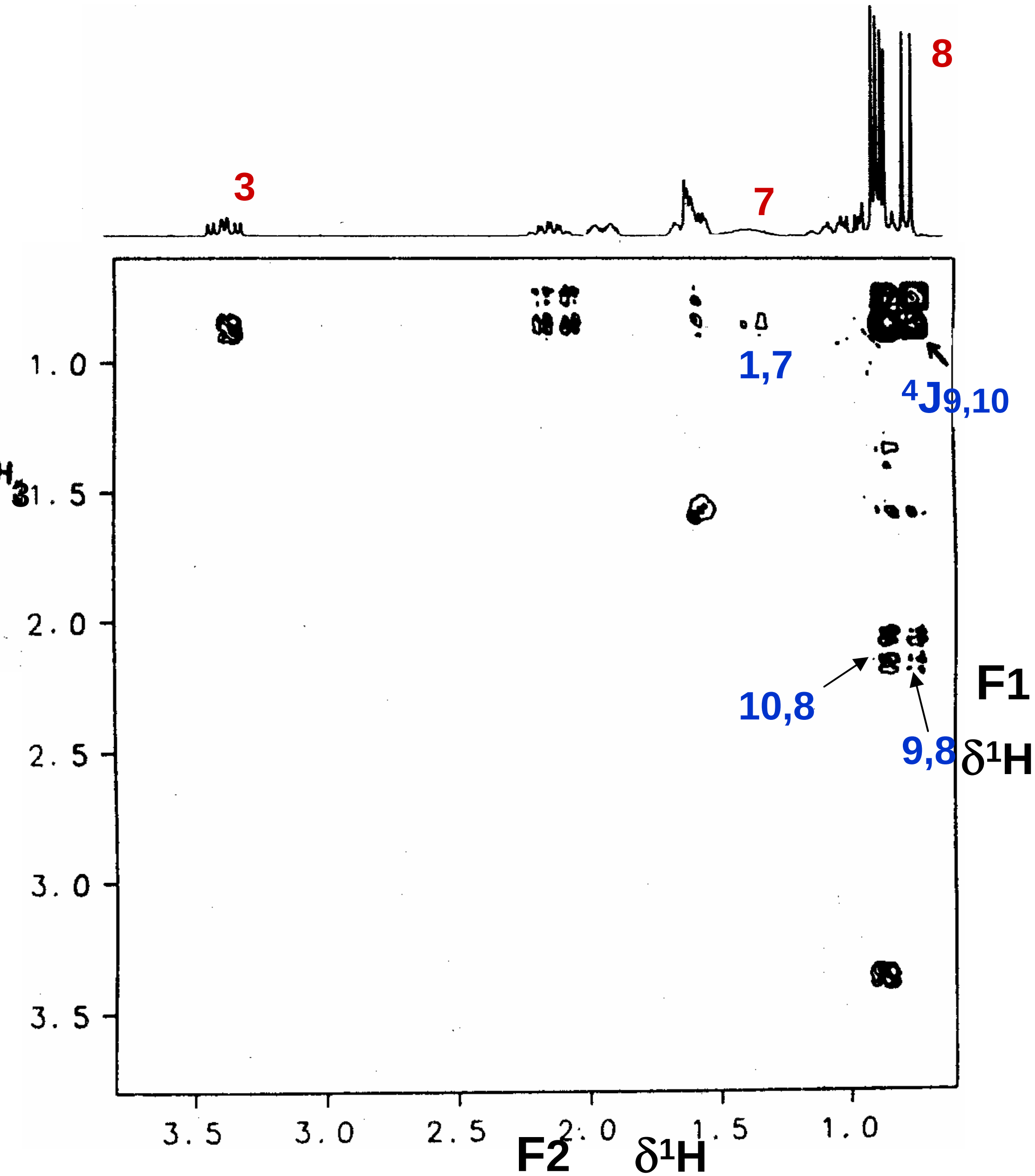
Assigning $^1H,^1H$ COSY Spectrum of Menthol



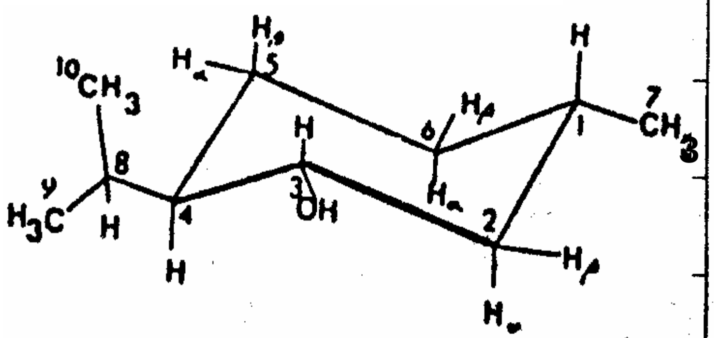


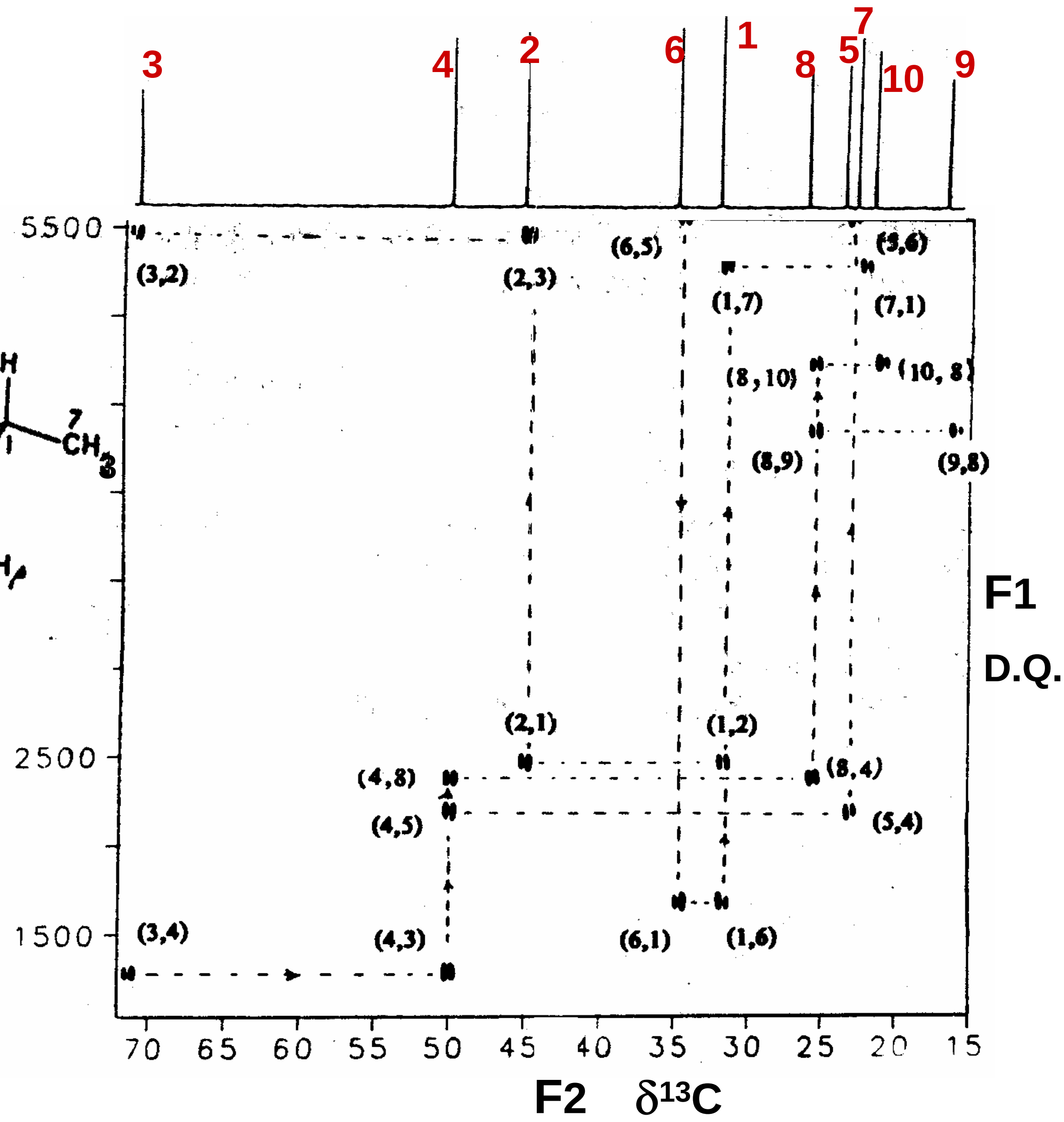
Assigning Long range $^{1}H,^{1}H$ COSY Spectrum of Menthol



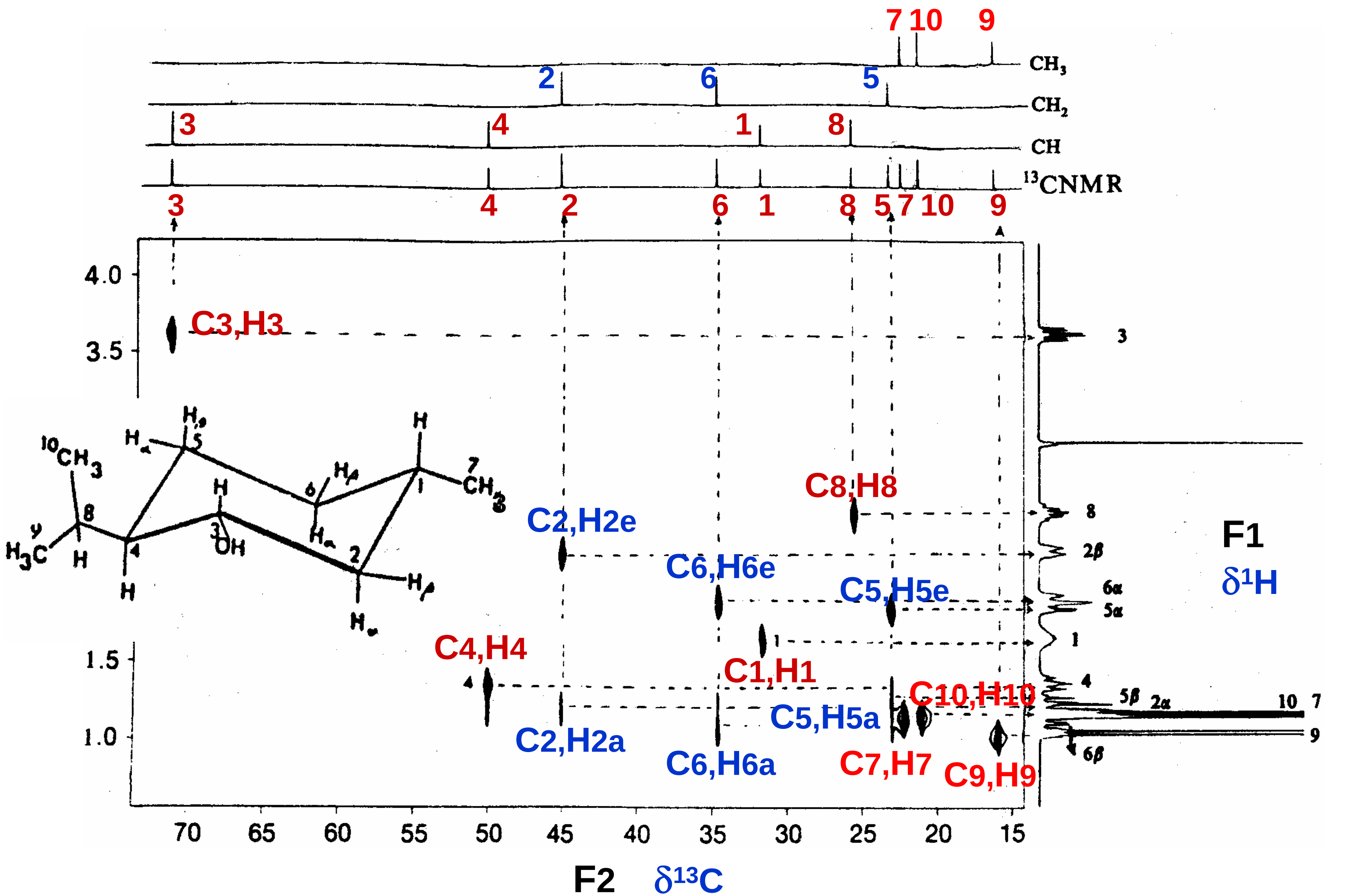


Assigning INADEQUATE Spectrum of Menthol

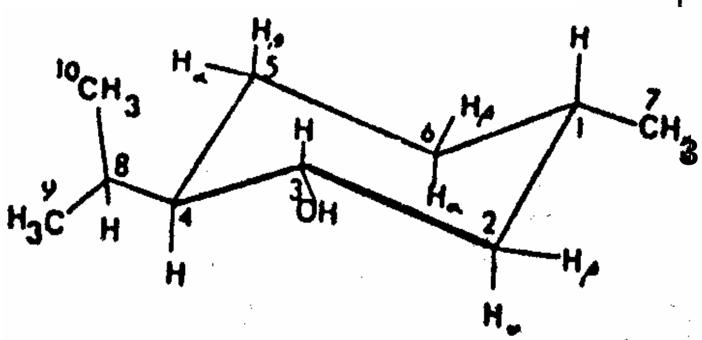


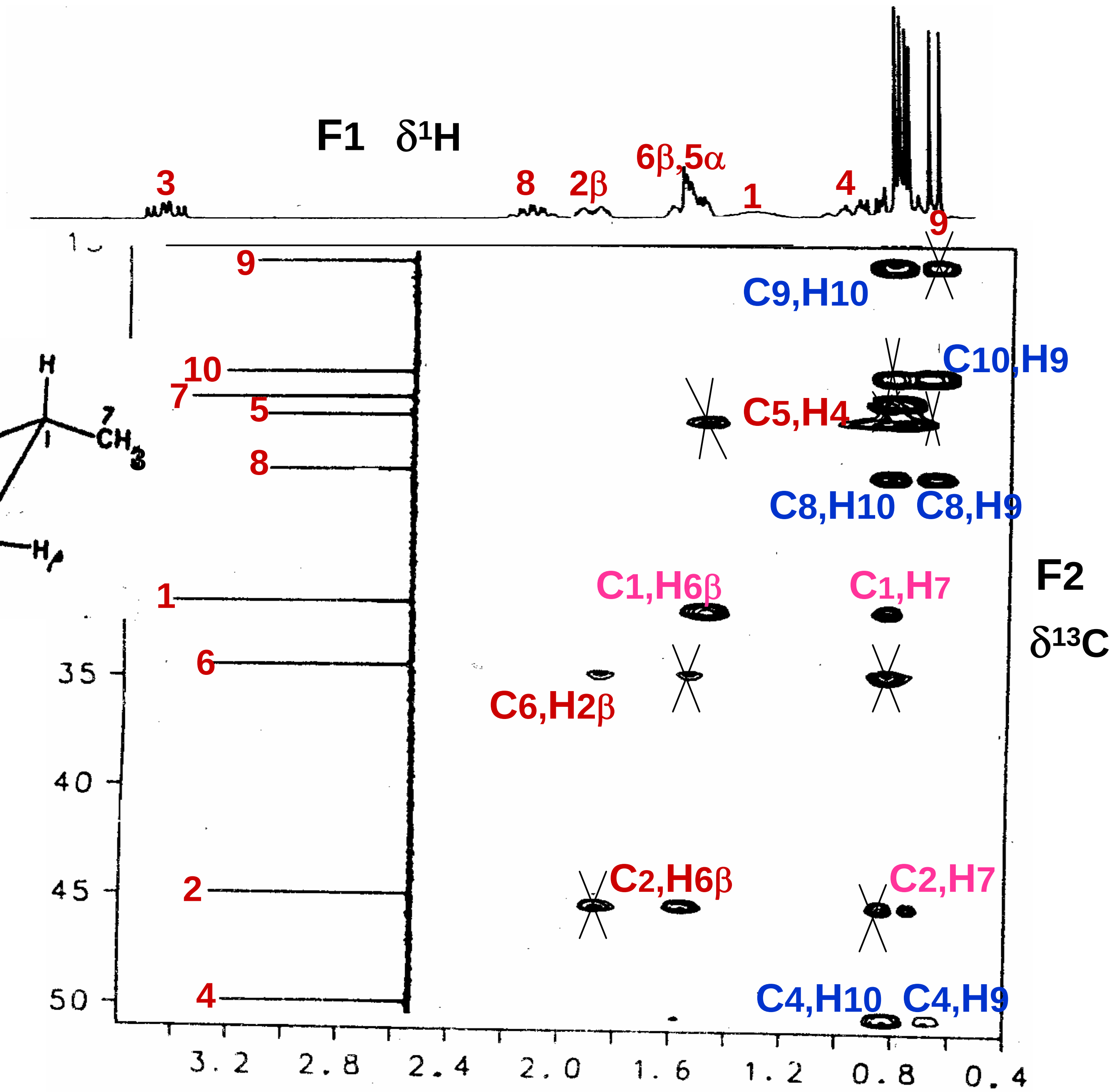


Assigning $^{13}C,^{1}H$ COSY Spectrum of Menthol

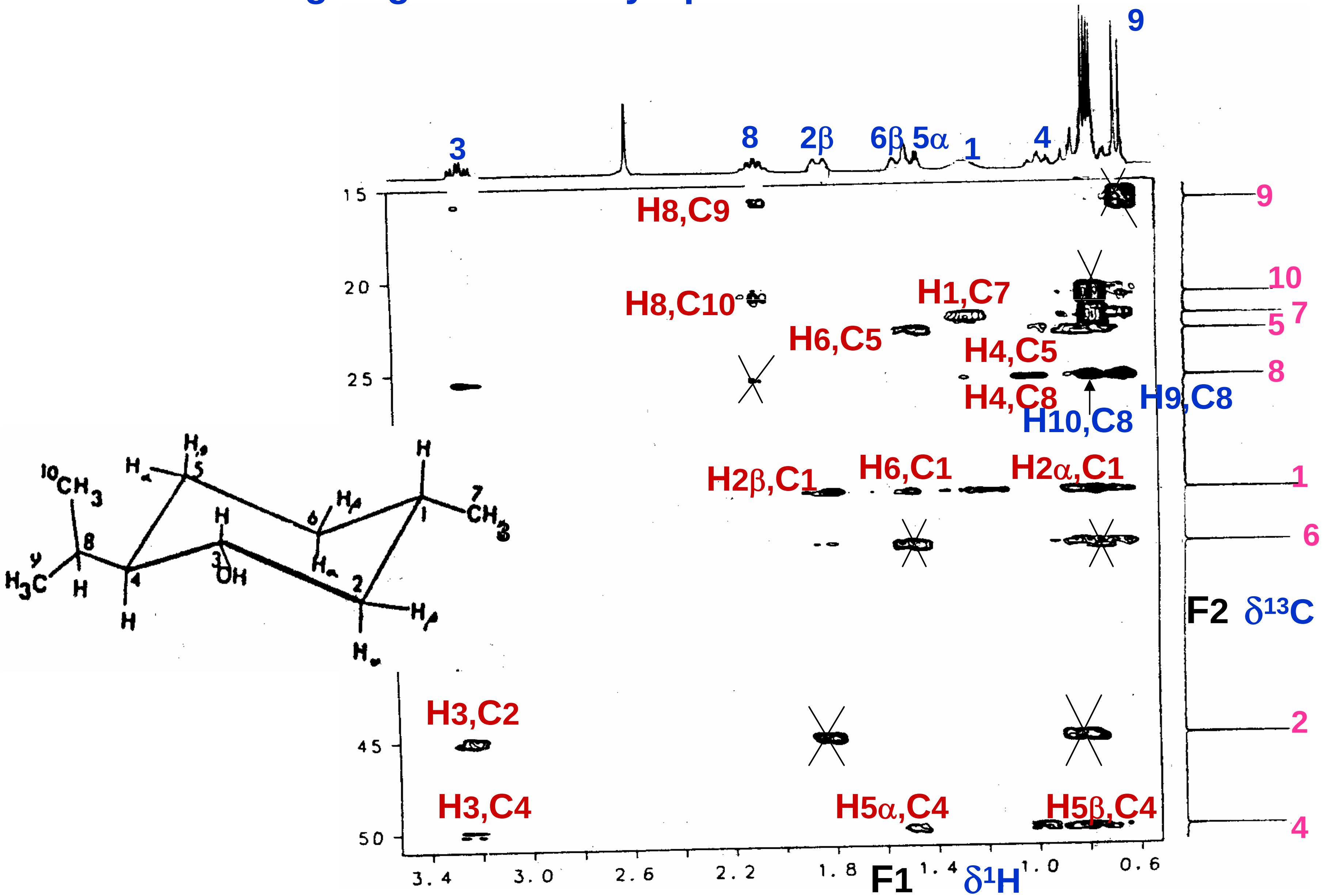


Assigning Long-range $^{13}C,^{1}H$ COSY (COLOC)

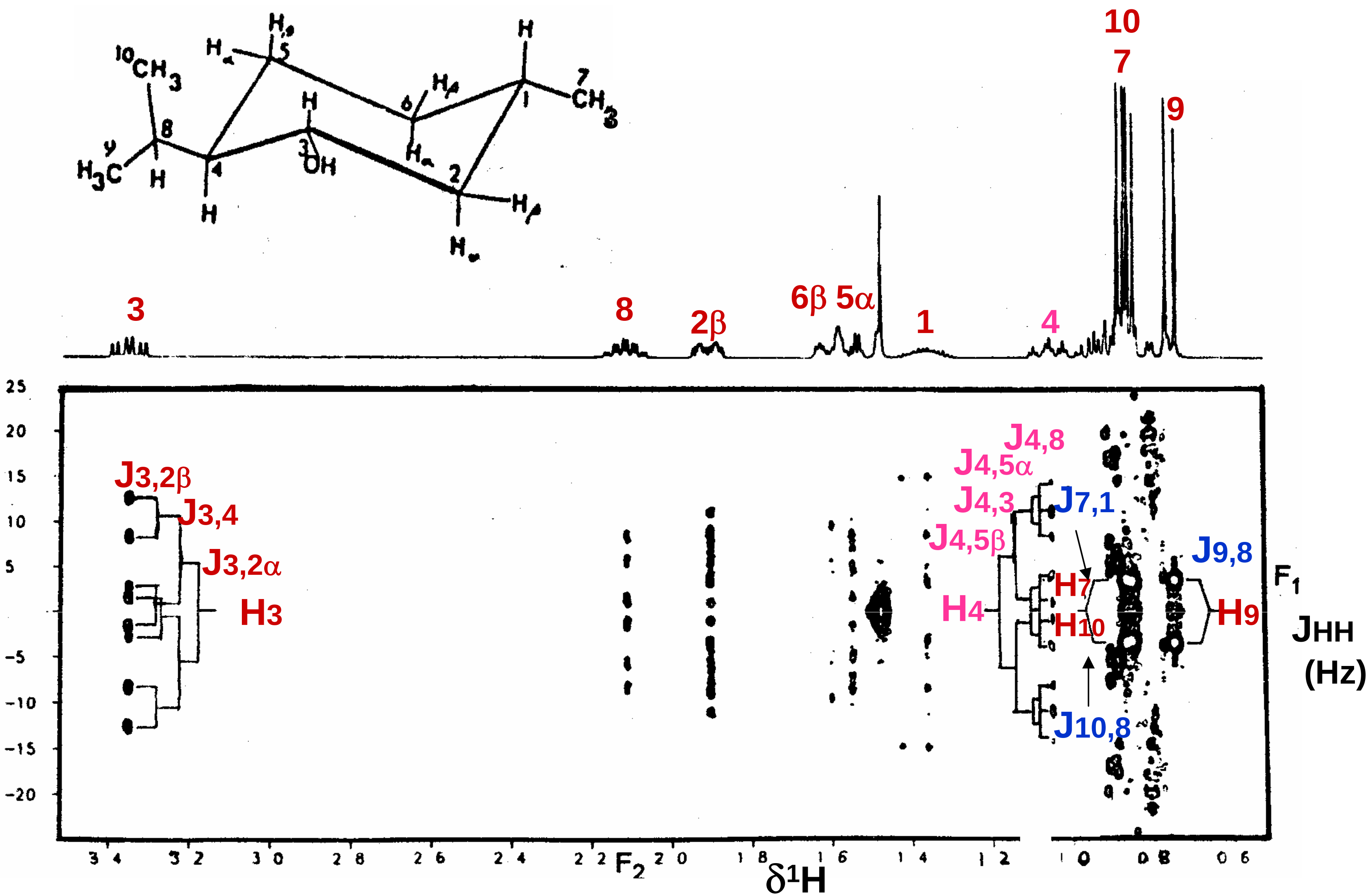




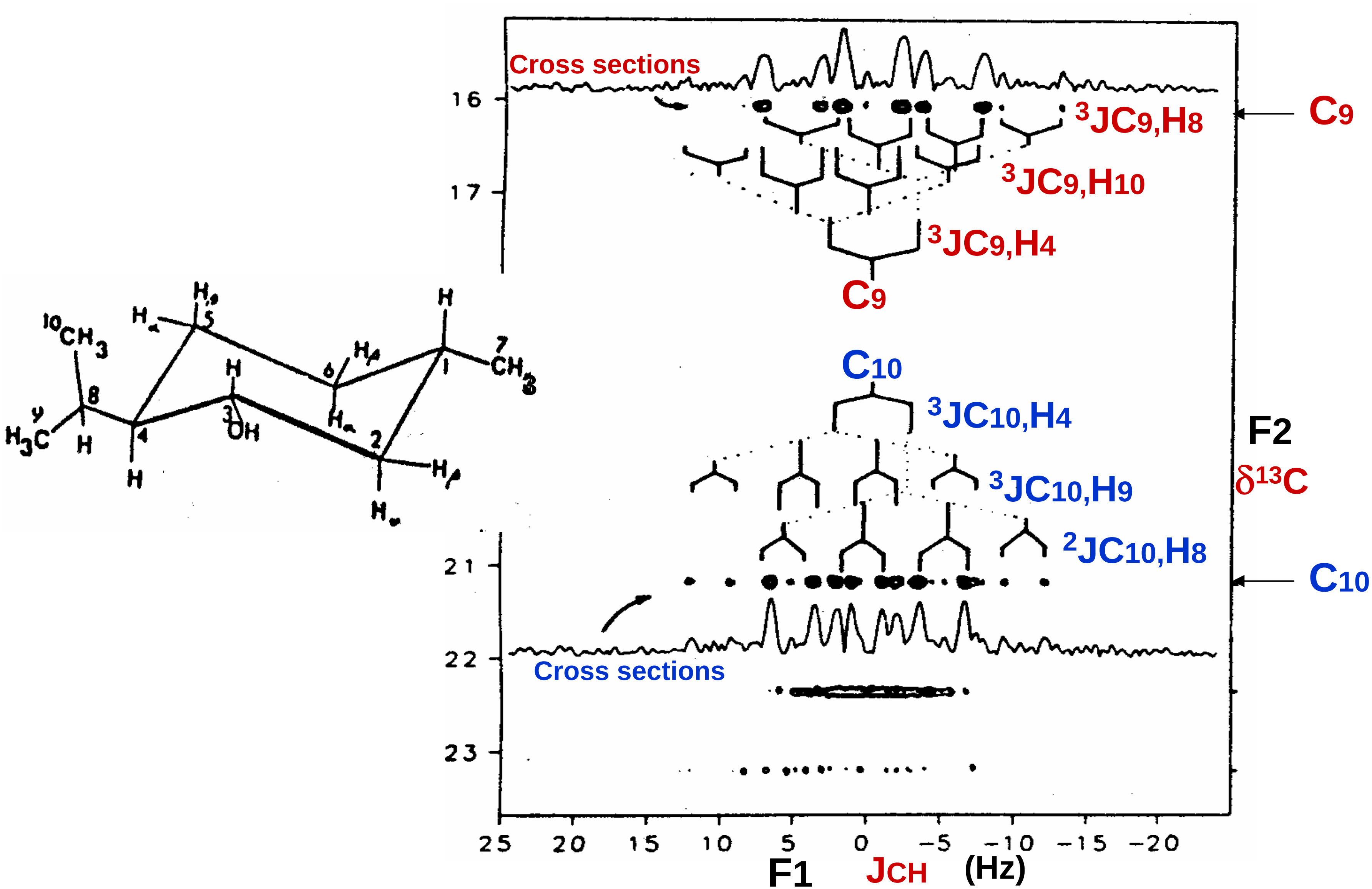
Assigning H-H-C Relay Spectrum of Menthol



Assigning $^1H,^1H$ 2D J- δ Spectrum of Menthol



Assigning Long-range ^{13}C,^{1}H 2D J- δ Spectrum of Menthol



三种菊科植物化学成分及其生物活性研究

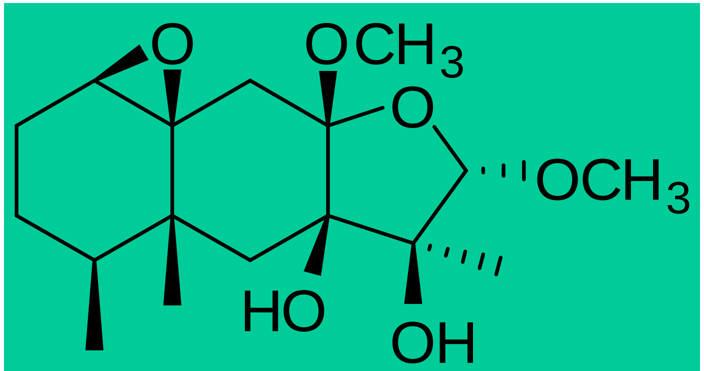


黄冬青

导师：高坤 教授

2007年12月4日

代表性化合物的结构解析

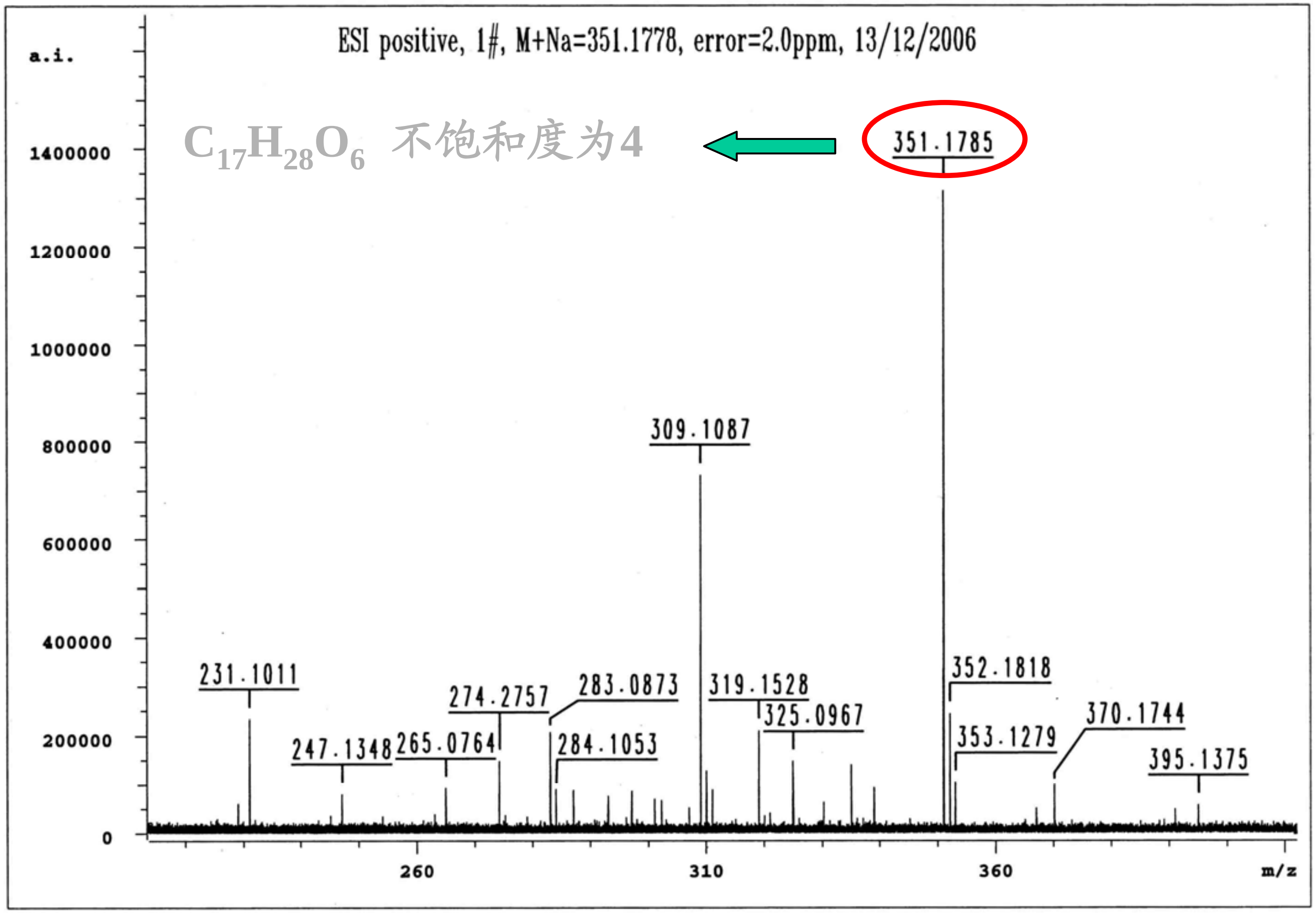


1

Colorless crystals (acetone), m.p. 96-98℃; $[\alpha]_{20}^{D}$: +82° (c 0.60, $CHCl_3$)

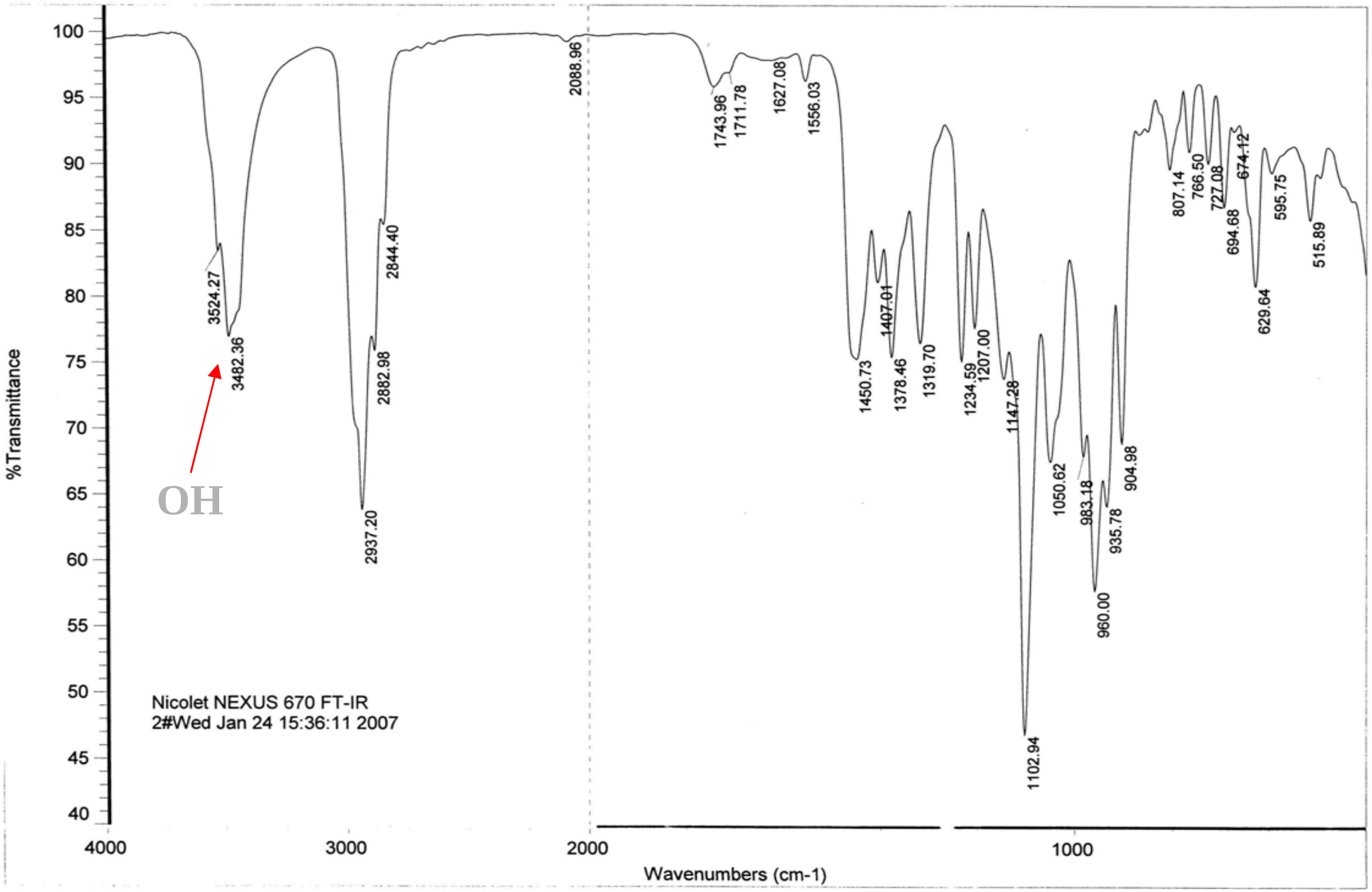
1*β*,10*β*(8,12)-diepoxy-7*β*,11*β*-dihydroxy-8*β*,12*α*-dimethoxyeremophilane

化合物的HRESIMS

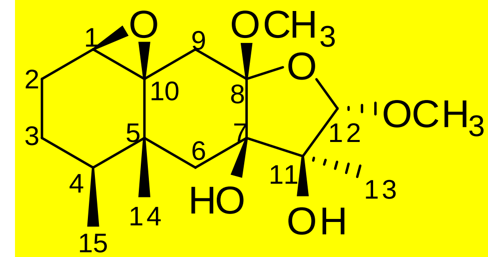


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化合物的IR

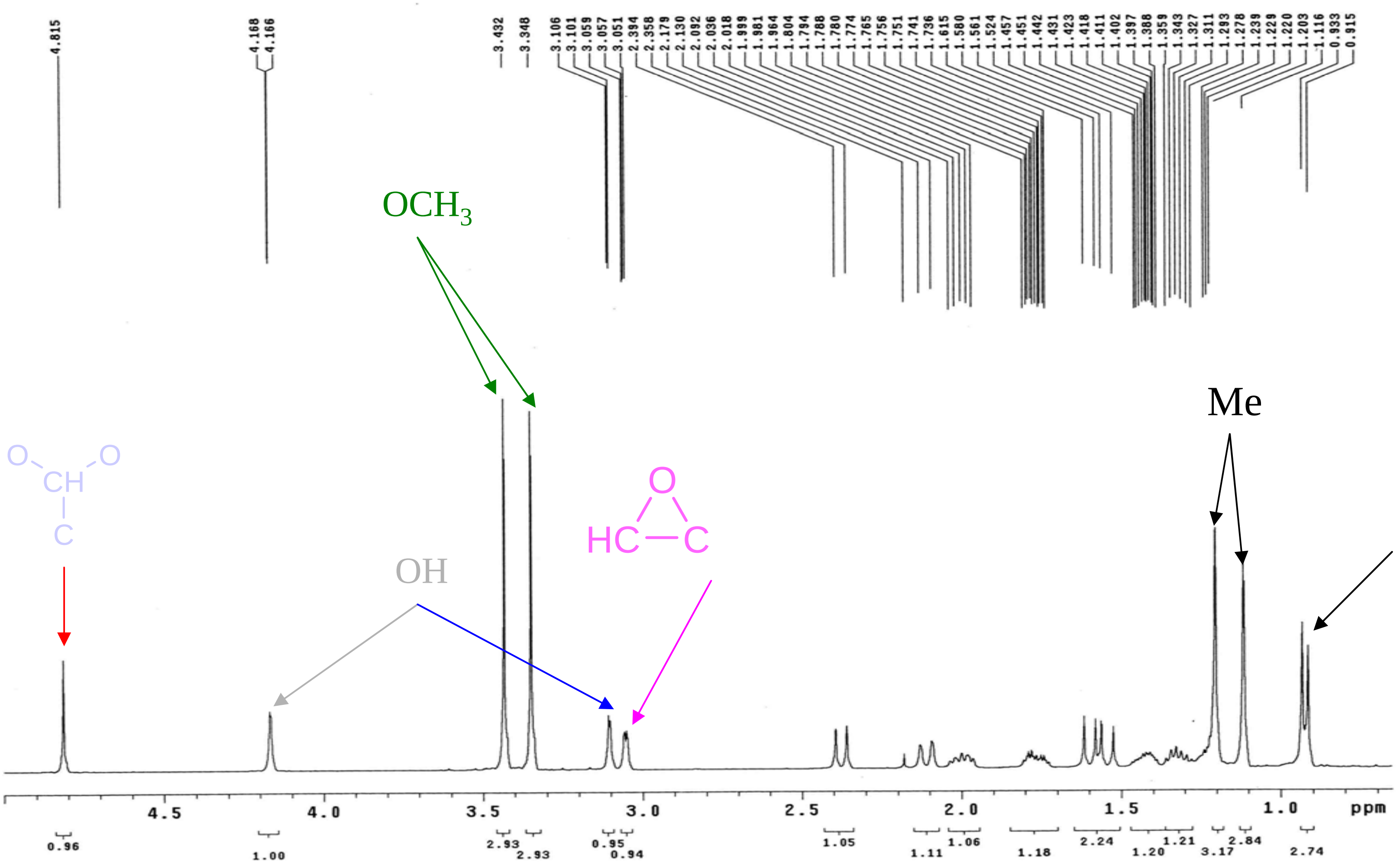


%Transmittance
100
95
90
85
80
75
70
65
60
55
50
45
40
4000
3000
2000
1000
Wavenumbers (cm-1)
OH
3524.27
3482.36
2937.20
2882.98
2844.40
2088.96
1743.96
1711.78
1627.08
1556.03
1450.73
1407.01
1378.46
1319.70
1234.59
1207.00
1147.28
1102.94
1050.62
983.18
960.00
935.78
904.98
807.14
766.50
727.08
694.68
674.12
629.64
595.75
515.89
Nicolet NEXUS 670 FT-IR
2#Wed Jan 24 15:36:11 2007

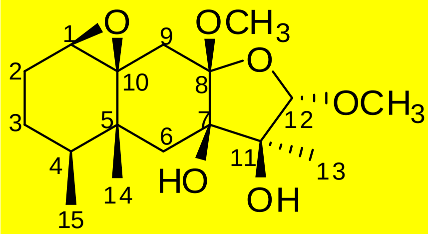


O
OCH3
O
OCH3
HO
OH
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

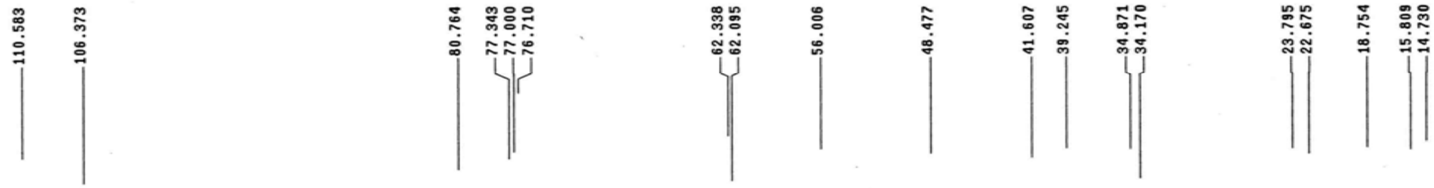
化合物的^{1}H NMR



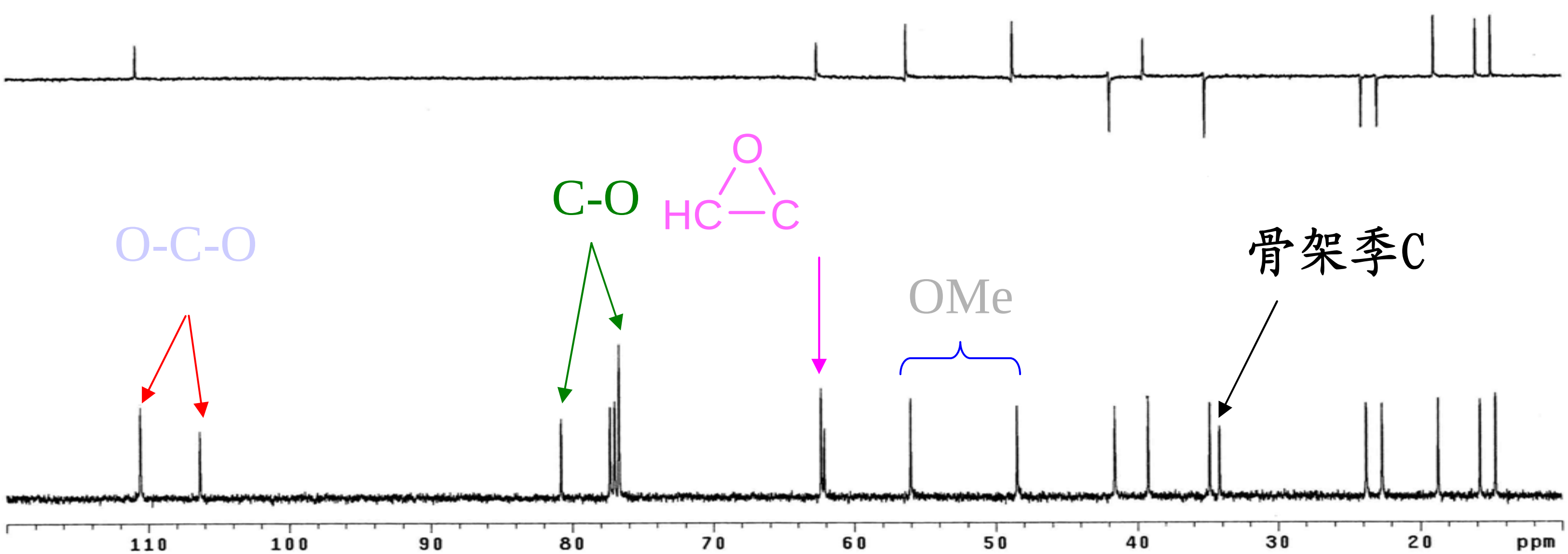
4.815
4.168
4.166
3.432
3.348
3.106 3.101 3.059 3.057 3.051 2.394 2.358 2.179 2.130 2.092 2.036 2.018 1.999 1.981 1.964 1.804 1.794 1.788 1.780 1.774 1.765 1.756 1.751 1.741 1.736 1.615 1.580 1.561 1.524 1.457 1.451 1.442 1.431 1.423 1.418 1.411 1.402 1.397 1.388 1.359 1.343 1.327 1.311 1.293 1.278 1.239 1.229 1.220 1.203 1.116 0.933 0.915
OCH3
O
CH
C
O
OH
O
HC
C
Me
Me
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.96
1.00
2.93
2.93
0.95
0.94
1.05
1.11
1.06
1.18
2.24
1.20
1.21
3.17
2.84
2.74



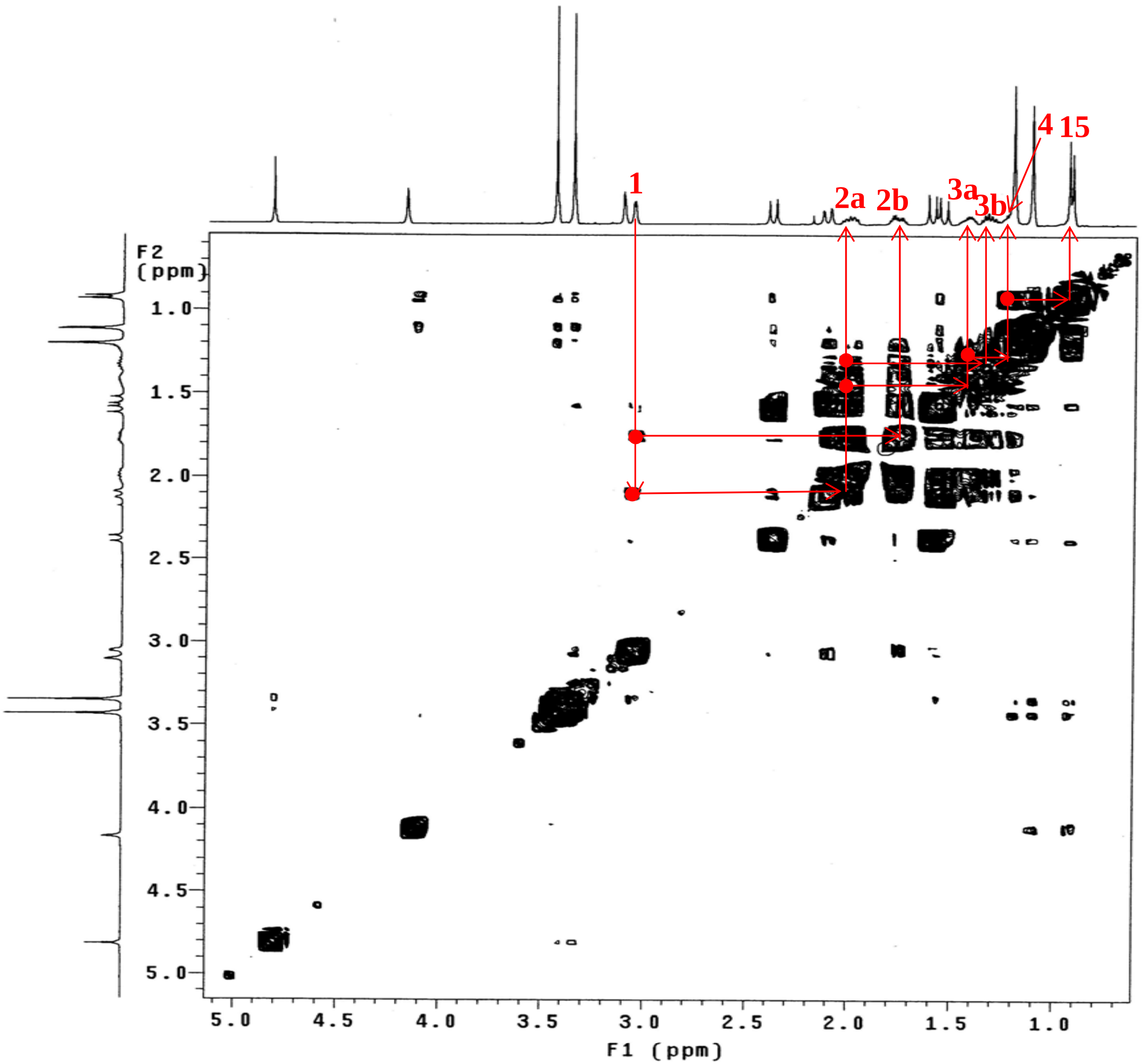
化合物的^{13}C NMR

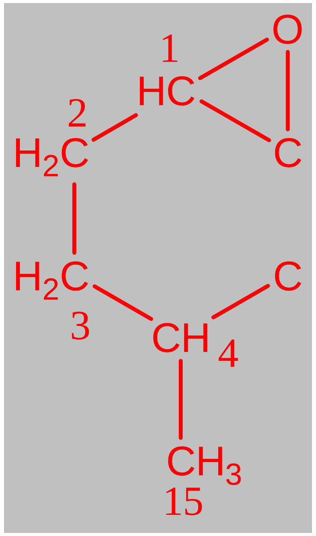


^{13}C NMR谱中含有17个碳信号(CH_3 × 3，CH_2 × 4, CH × 3, C × 5, OMe × 2)，除去2个OMe信号，还有15个碳信号，表明可能为一个倍半萜结构。

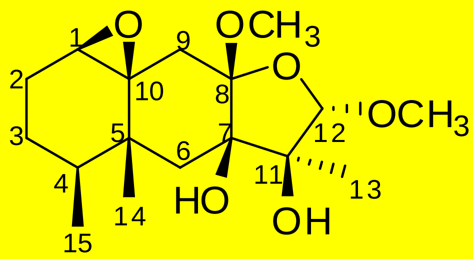


化合物的^{1}H-^{1}H COSY





片断1



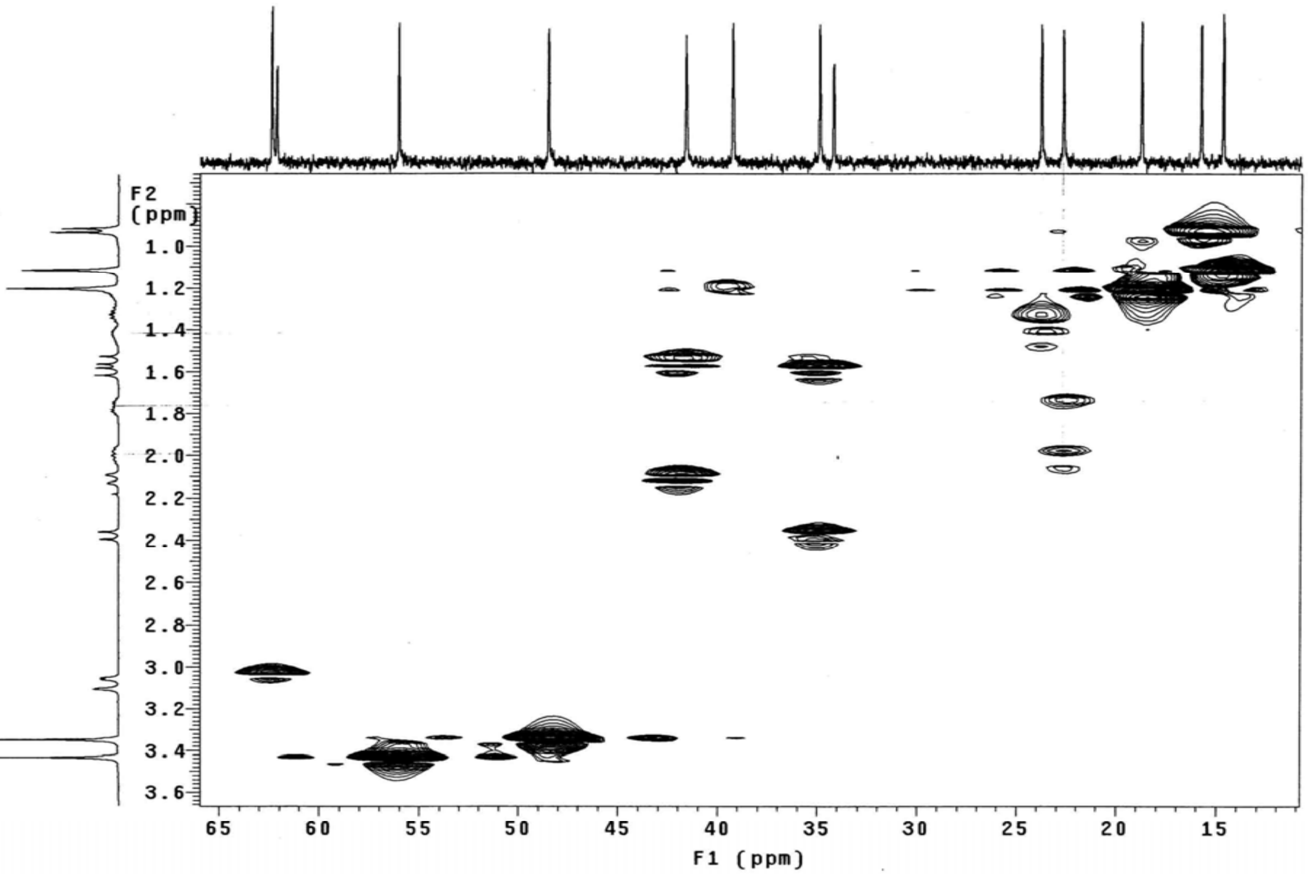
化合物的HSQC

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STANDARD 1H OBSERVE

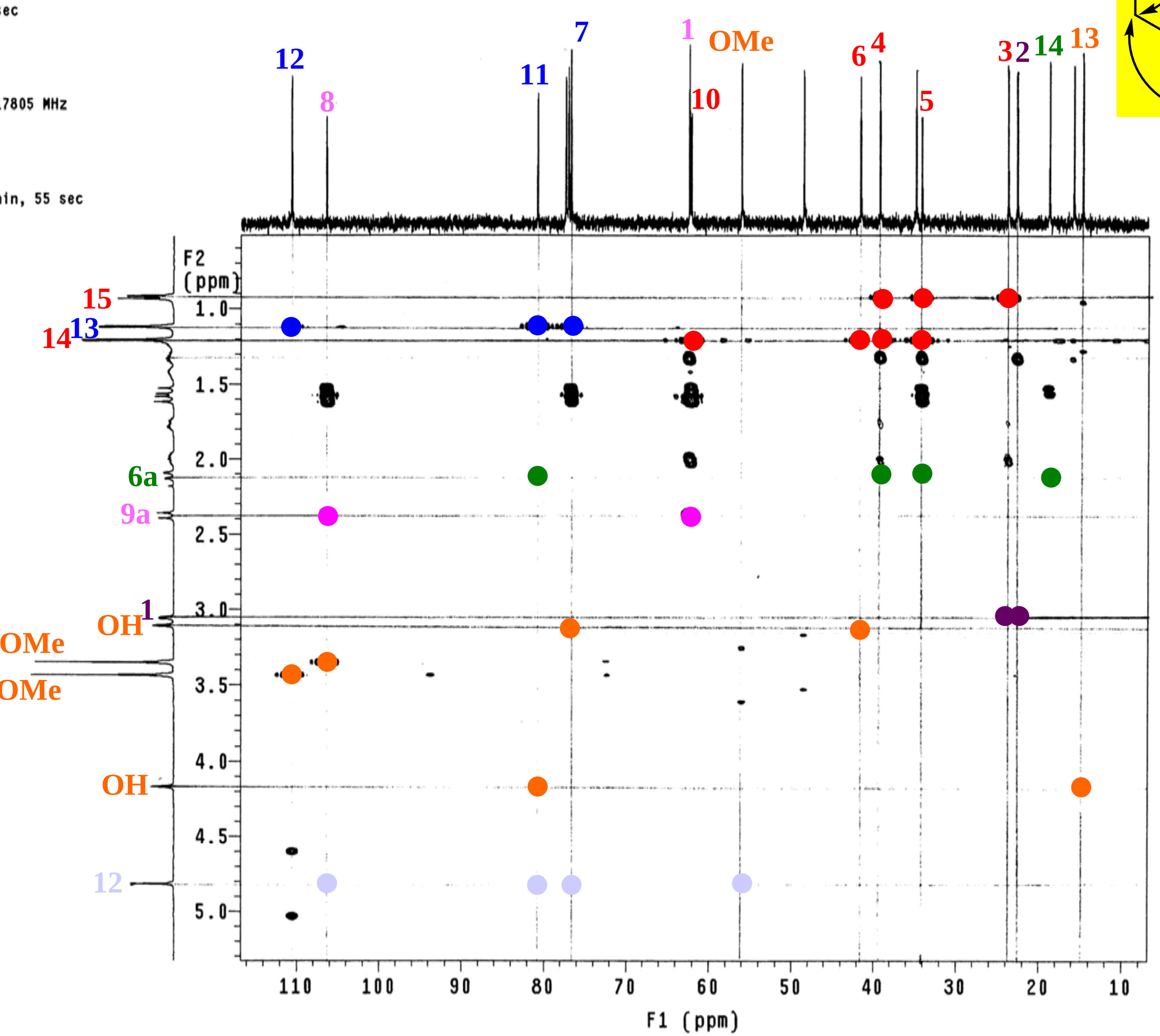
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 Sample directory:
 File: PROTON

Pulse Sequence: gHSQC
 Solvent: CDCl3
 Ambient temperature
Mercury-400BB  "ULAOC400"

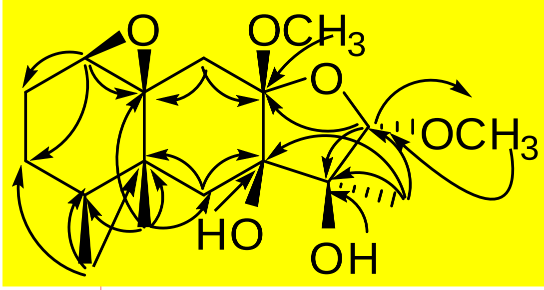
 Relax. delay 1.000 sec
 Acq. time 0.160 sec
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 2D Width 17094.0 Hz
 32 repetitions
 2 x 128 increments
OBSERVE   H1, 400.1717870 MHz
DECOUPLE C13, 100.6308056 MHz
 Power 48 dB
 on during acquisition
 off during delay
 GARP-1 modulated
DATA PROCESSING
 Gauss apodization 0.074 sec
F1 DATA PROCESSING
 Gauss apodization 0.014 sec
FT size 2048 x 2048
Total time 2 hr, 55 min, 8 sec
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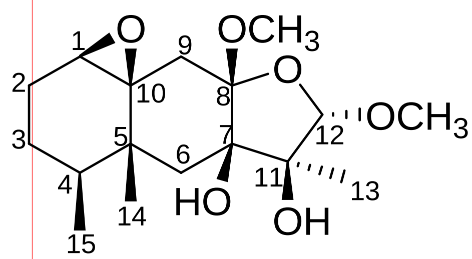
化合物的HMBC



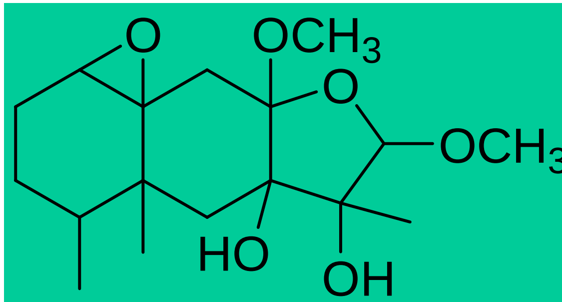
12
8
11
7
1
OMe
10
6
4
5
3
2
14
13
15
14
13
6a
9a
OH
1
OMe
OMe
OH
12
F2 (ppm)
F1 (ppm)



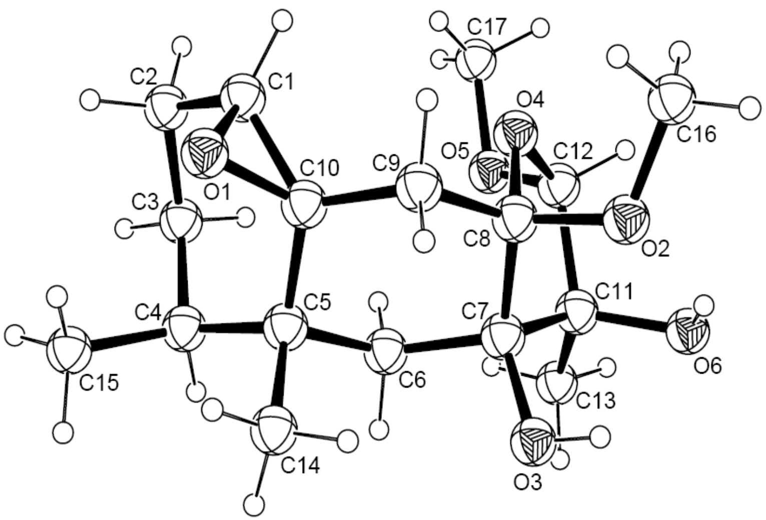
O
OCH_3
O
OCH_3
HO
OH

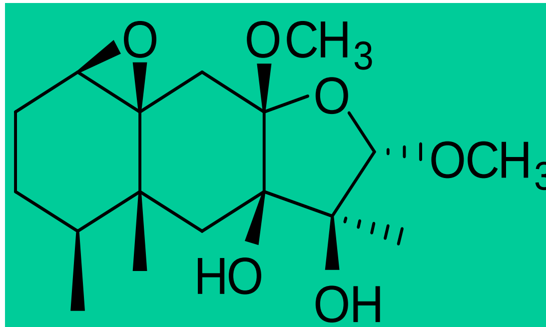


1
O
9
OCH_3
O
2
10
8
OCH_3
3
5
7
12
6
4
11
13
HO
14
OH
15



1





1

1β,10β(8,12)-diepoxy-7β,11β-dihydroxy-8β,12α-dimethoxyeremophilane